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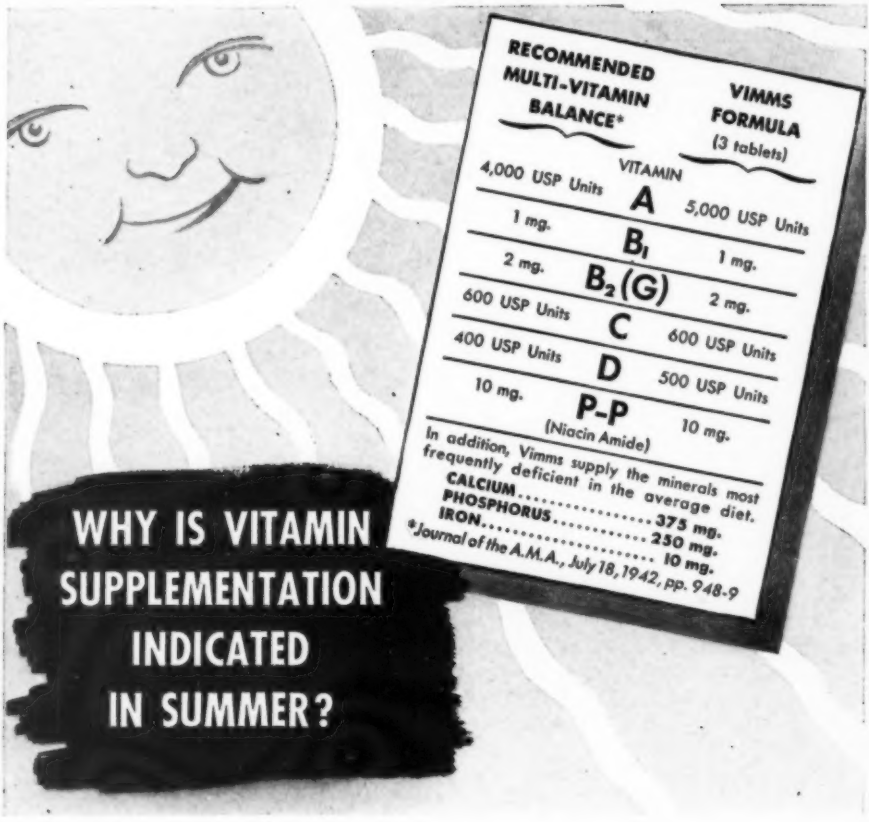
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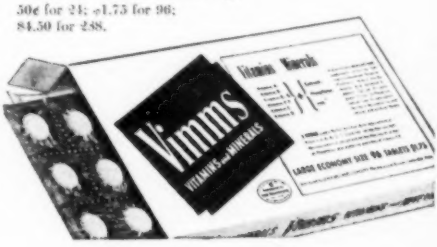

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The Journal of Pediatrics

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Original Communications

STOMATITIS AND DIARRHEA OF INFANTS CAUSED BY A HITHERTO UNRECOGNIZED VIRUS

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STOMATITIS of infants and children has been of great interest and has received special attention in the pediatrics outpatient department and wards of the Vanderbilt University Hospital for the past several years. In 1938, experimental investigations were reported which showed that in many cases of primary stomatitis in children the virus of herpes is the causative agent.[1] These observations were subsequently confirmed by Burnet and Williams.[2] Since June of 1942, a type of stomatitis of infants has been frequently observed which differs markedly from any type previously encountered. An atypical form of herpetic stomatitis was at first suspected. Swabbings obtained from the mouths of infants and children with the condition have consistently failed to produce herpetic keratitis in the eyes of rabbits. However, a definitely recognizable reaction, which differs from and does not produce immunity to herpes, has been repeatedly induced in rabbit eyes by inoculation of the scarified cornea. The infectious agent which has proved to be filterable through Berkefeld V candles has been propagated by means of serial passage in rabbit eyes. The evidence thus far obtained indicates that it is a virus which has hitherto been unrecognized. Although many details regarding the nature and behavior of this pathogenic agent are still being investigated, sufficient data have accumulated to justify a report of the clinical characteristics of the disease and of the experimental findings thus far obtained.

CLINICAL CHARACTERISTICS OF THE DISEASE

The majority of the cases have been observed in infants under 6 months of age. The disease has affected infants as young as 3 days, children up to 8 years of age, and an occasional adult. The mothers com-

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plain that the child has a sore mouth and that he refuses to take feedings well. He usually has little or no fever but is fretful and irritable. On examination it is found that the lip, anterior margin, and under surface of the tongue is fiery red in color. During the first and second day of the disease numerous delicate vesicles are present in the affected area and may also be found scattered on the gums and on the inner surface of the lower lip. Later the mucous membrane of the tongue desquamates leaving a raw surface which bleeds readily. In older children and in infants who have teeth there is a more marked involvement of the gums with vesicles, shallow ulcerations, and marked swelling. Salivation is, in most instances, moderately increased but an occasional infant has an extremely dry mouth. Many of the infants suffer from a moderate diarrhea. The stools are frequent, contain large quantities of mucus and sometimes flecks of bright red blood. The disease, in most instances, lasts from three to ten days but apparent recovery is often followed by one or more relapses so that it may be at least two months before the child is entirely well. The disease is contagious and the incubation period apparently short. The disease was noted in the second of a pair of twins three days after the onset of symptoms in the first twin and secondary cases occurred on the hospital ward within two to three days after the admission of an infant sick with the disease. Mouth washes of various kinds, painting with gentian violet, and the administration of sulfonamides have no apparent influence on the course of the infection.

The condition has thus far been observed in fifty-three children seen in the outpatient department, the children's ward, and in private practice. Swabbings from the mouth of forty-five of the children have been inoculated onto the scarified cornea of a rabbit and have all produced a characteristic reaction. Swabbings of the stools of twelve of the children who had diarrhea as well as stomatitis produced similar lesions on the rabbit's cornea. Of the forty-five children, twenty-eight were 6 months of age or younger, nine were from 6 months to 1 year, five from 1 to 2 years of age, and one each of 4, 5, and 8 years respectively.

During the month of October, 1943, one of a pair of premature twins in the nursery for newborn infants was found to have stomatitis and diarrhea. Within the next few days several other infants developed the infection. In spite of immediate strict isolation precautions, sixteen of thirty infants in the nursery developed diarrhea within the course of the next two weeks. Although a mild stomatitis was present in ten of the sixteen infants, the outstanding feature of the disease was diarrhea with the daily passage of four or five green stools composed largely of mucus. The majority of the babies continued to take their feedings and to gain weight satisfactorily. Four premature infants, who had more frequent and more watery stools than the full-term infants, became dehydrated and developed an acidosis. They were transferred to the pediatric ward where they promptly improved after treatment of their condition with a period of starvation and the administration of parenteral fluids.

Swabs obtained from the mouths and stools of all of the sixteen affected infants produced characteristic lesions when inoculated onto the cornea of a rabbit. Swabs from the fourteen unaffected babies produced no lesion. In the majority of instances the diarrhea began when the infants were 4 or 5 days of age. Two infants who had previously been proved to be free of infection in their first week of life developed the disease when they were 11 and 14 days old respectively.

EXPERIMENTAL

Experimental infection of rabbit eyes.—Because this disease was at first considered as a possible atypical form of primary herpetic stomatitis, the method employed in the identification of herpes virus by producing keratitis in rabbits was followed. Dry sterile cotton swabs on wood applicator sticks were lightly wiped over the involved areas on the tongue and gums of the infants. When the stools were tested a small amount of fecal material was picked up by means of the same type of swab. If the stools were not available, a swab was introduced into the anus. The swabbings were inoculated onto rabbit corneas as soon as possible after collection. If storage overnight in the refrigerator was necessary, a small amount of normal saline was placed in the test tubes containing the swabs to prevent drying. Rabbits, preferably 6 weeks to 6 months of age were anesthetized, the eyes "popped," and the cornea scarified by means of a sharp dissecting needle. The swab was then rubbed lightly over the scarified cornea.

When this technique is employed, a reaction develops within twenty-four hours. The cornea becomes definitely hazy, with cloudiness along the lines of scarification. The sclera is injected. The palpebral conjunctiva becomes markedly injected and swollen and a small amount of pus collects at the inner canthus. In many instances a severe iritis develops. The cloudiness of the cornea with swelling and injection of the conjunctiva persists and increases in severity for about forty-eight to sixty hours and then rapidly recedes, leaving a normal appearing eye after from seventy-two to ninety-six hours. A few fine scars usually persist permanently along the deeper lines of scarification. Purulent keratitis with complete permanent opacity of the cornea typical of herpetic keratitis does not develop.

Reactions having these gross characteristics have been obtained in rabbit eyes following inoculation of mouth swabbings from each of the forty-five children with stomatitis and with stool swabs of each of twelve having an accompanying diarrhea. The same type of reaction was obtained from both the mouth and stool swabs from the sixteen infants who developed diarrhea while in the nursery during October, 1943. During the period of investigation swabbings from sixteen children with thrush, nonspecific mouth lesions, Vincent's infection, or normal mouths failed to produce this type of reaction. From the fourteen of the thirty infants in the nursery who did not develop diar-

rhea or stomatitis during the October epidemic, mouth and stool swabs produced only a temporary slight inflammatory reaction in rabbit eyes which rarely lasted more than twenty-four hours. Swabs from the mouths of fourteen children diagnosed as having herpetic stomatitis produced typical herpetic keratitis in rabbit eyes during the period of investigation.

Cultures of the mouth swabs on various bacterial media revealed the usual type of mouth flora and no specific bacterium could be implicated. Inoculation of rabbit eyes with suspensions of bacterial cultures obtained from the mouths of several of the patients failed to produce the reaction. Stool cultures from the patients with diarrhea were consistently negative for the usual intestinal bacterial pathogens. Corneas removed and ground aseptically at the forty-eight-hour period of the reaction and cultured aerobically and under anaerobic conditions were in the majority of instances sterile. Occasionally a few colonies of staphylococci or diphtheroids were recovered.

Propagation of the causative agent by serial passage in rabbit eyes.—Difficulty was at first experienced in transferring the infectious agent beyond the first or second transfer. This was overcome by using young rabbits from 6 to 12 weeks of age. Infected corneas are removed at the forty-eight-hour period, ground with sterile alundum and suspended in 1 to 3 c.c. of normal saline. This suspension is then transferred to the scarified corneas of young rabbits. In this manner the agent has been propagated up to the present through forty successive passages in rabbit eyes. The gross reaction has been typical in every respect at each passage.

Microscopic characteristics of the reaction in rabbit eyes.—Infected eyes from rabbits sacrificed at twenty-four and forty-eight hours were fixed in Zenker's solution, embedded in paraffin, sectioned and stained with hematoxylin and eosin. Selected sections were stained with phloxine and methylene blue and by Goodpasture's carbol-aniline fuchsin method. Samples for section were obtained from fifteen separate patients and from several of the serial passages. All the eyes show the development of the same type of reaction. It is characterized by a focal destruction of corneal epithelium with an intense acute inflammatory reaction and areas of focal necrosis in the substantia propria of the cornea. There is usually a separation of the inner mesothelial lining of the cornea from its basement membrane and many polymorphonuclear cells collect within this space. Inflammatory cells are present in small numbers in the aqueous humour and usually collect in large numbers at the junction of the cornea and iris. In many instances the iris is swollen and numerous polymorphonuclear cells have wandered into the intercellular spaces. Intracytoplasmic or intranuclear inclusion bodies have not been observed at any stage of the reaction. Sections stained with carbol-aniline fuchsin have not revealed the presence of bacteria in the lesions.

Filterability of the infectious agent.—On five separate occasions pooled suspensions of ground infected corneas were subjected to filtration through Berkefeld V candles. The filtrate was then spun in the angle centrifuge at 3,000 revolutions per minute for one and one-half hours. The supernatant was poured off, leaving a small pellet of grayish blue sediment in the bottom of the tube. This was resuspended in a small amount of saline and inoculated onto rabbit corneas. A typical reaction developed in each instance. These rabbits were later found to be immune to reinfection with this virus and subsequently susceptible to infection with herpes virus.

Immunity reactions in rabbits.—After a strain of the virus was established in serial passage, reinoculation experiments were performed. Four to six weeks after the primary reactions twenty-three rabbits inoculated with material obtained from the mouths of each of twenty-three children with stomatitis and six rabbits infected with the passage material were reinoculated with infected corneal suspension. All the animals were found to be refractive to reinfection. The rabbits of this series were subsequently inoculated with a strain of herpes H. F. virus. All developed typical herpetic keratitis.

Neutralization of the virus by convalescent serum from patients.—Blood for serum was drawn from sixteen patients during the acute stage of the disease and again from two to six weeks later. Titrations of infected corneal suspensions were first run to determine the highest titer which would produce a good reaction in rabbit eyes. In some tests suspensions corresponding to a dilution by volume of 1-200 and in others to 1-500 of the infected cornea were mixed in equal amounts with undiluted acute and convalescent serum. After incubating the mixtures at 37° C. for an hour they were stored in the refrigerator overnight. The mixtures were then inoculated by means of sterile swabs onto scarified rabbit corneas. The convalescent serum completely inhibited the development of a reaction in rabbit eyes while the acute serum-virus mixtures obtained from each of twelve patients tested produced positive reactions of the cornea.

Neutralization of herpes virus by convalescent serum from patients.—Patients with primary herpetic stomatitis develop neutralizing antibodies for herpes virus during the course of the disease.[2] The acute and convalescent serum of sixteen of the patients in this series were tested for the presence of herpes neutralizing antibodies by the pock-counting technique on the chorio-allantois of chick embryos. No antibodies to herpes were present in the acute or convalescent serum of thirteen patients. In three cases antibodies to herpes were found to be present in the acute serum with no increase in their titer in the convalescent serum.

Accidental laboratory infection in an adult.—During the course of various experimental procedures with the virus intracorneal inoculation of rabbits with Berkefeld V filtered corneal suspension was at-

tempted. While injecting a suspension corresponding approximately to a 1-5,000 dilution of the original corneal suspension from the thirty-third passage in rabbit eyes, one of us (G. J. B.) accidentally received a small amount of the infectious material directly into the mouth. On the third day moderate malaise and headache developed. Later in the day the tip and anterior edges of the tongue became painful and felt as if they had been scalded. The mucous membranes of the lips became markedly swollen and red. The tip, anterior edges, and under surface of the tongue were fiery red. Numerous fine vesicles were present on the affected area of the tongue and the mucous membranes of the lips. No fever developed. The following day there was widespread desquamation of the epithelium of the mucosa of the lips. The subjective symptoms were much improved. By the fourth day after onset of symptoms the mouth was again normal. No diarrhea developed. Swabs obtained from the mouth lesions produced a typical reaction in rabbit eyes. Mouth washings in 50 per cent broth and saline were passed through a Berkefeld V candle. The filtrate was spun in the angle centrifuge for one and one-half hours at 3,000 revolutions per minute and the sediment inoculated onto rabbit corneas. Typically positive reactions developed. Mouth swabbings obtained on the fourth day after onset produced no reaction in rabbit corneas. Neutralization tests set up with serum obtained on the first day of the disease and serum obtained three weeks later showed that the convalescent serum completely inhibited the reaction. The acute serum did not contain neutralizing antibodies for the virus.

Attempts to produce diarrhea experimentally in rabbits.—The experimental production of diarrhea in young rabbits from 4 to 6 weeks of age by feeding them suspensions of rabbit cornea infected with the virus has been attempted. On two occasions groups of two rabbits each have developed diarrhea seven days after feeding them 1 c.c. of a 1-10 saline suspension of infected rabbit cornea. Rabbits from the same litter fed suspensions of normal cornea in the same manner did not develop diarrhea. The animals developing diarrhea were found when sacrificed to have numerous shallow ulcerations in the lower ileum and cecum. A marked increase in the amount of mucus was noted in the intestine. Inoculation of intestinal contents onto the eyes of normal rabbits produced reactions typical of those produced by the virus. Attempts to transfer the diarrhea by feeding the intestinal contents to other rabbits were unsuccessful. On three other occasions attempts to produce diarrhea by feeding young rabbits suspensions of infected cornea have failed. This aspect of the investigation is being continued in the hope of being able to reproduce the diarrhea at will.

Attempts to establish the virus in other experimental hosts.—The corneal reaction has been successfully reproduced in guinea-pig eyes but is not as typical or as clear-cut as in rabbit eyes. Injection of infected corneal suspension intracutaneously or subcutaneously in rab-

bits or guinea-pigs produces no recognizable reaction. It has not yet been possible to adapt the virus to propagation in the developing chick embryo.

The nature of the virus.—Thus far the virus has been passed only through Berkefeld V candles. Studies in regard to its size and nature are in progress. It seems to be quite resistant to outside influences. Suspensions of infected cornea in normal saline have been found to be active after ninety days of storage in the refrigerator at 0° C. Accurate studies as to infectivity titers of the virus await the development of a method more satisfactory than the use of the scarified rabbit corneas. Many other problems regarding the nature of the virus and the disease it produces require further investigations.

INVESTIGATION OF POSSIBLE SOURCE AND METHOD OF SPREAD OF THE INFECTIOUS AGENT

When the epidemic of diarrhea associated with the virus occurred in the nursery for newborn infants, attempts were made to discover the source and manner of spread of the infection. Mouth swabs from three of the four nurses in charge of the nursery were found to be positive for the virus producing typical reactions in rabbit eyes. Two of the three adults at no time had lesions in their mouths but one developed stomatitis during the week following the outbreak of diarrhea in the nursery. She carried the infection home to her two children, 6 and 8 years old. Both children developed stomatitis and swabbings from their mouths produced typical reactions in rabbit eyes. Three months later, at the time of the writing of this paper, mouth swabs from this nurse are still positive for the virus. Swabs from the other two nurses were negative two weeks after the nurses were removed from the nursery.

Mouth swabs from sixty adults who were more or less directly engaged in caring for the children in the nurseries and the pediatric wards were inoculated onto scarified rabbit corneas shortly after the time the diarrhea began in infants in the nursery. Two of the adults were found to be carrying the virus in their mouths without perceptible signs or symptoms of infection. One of these carriers was an intern who had taken charge of the nursery after the epidemic of diarrhea had ceased following the institution of strict isolation precautions and the employment of nurses who had been proved by inoculation of rabbit's eyes to be free of the virus. Four days after the new intern took charge of the nursery three new cases of stomatitis and diarrhea developed. Substitution of this intern by another who was known to be free of the virus and isolation of the three infected infants controlled further spread of the disease. The two adults from whose mouths virus had been demonstrated were found to be positive after two weeks but were negative one month later as determined by inoculating mouth swabs on rabbit's corneas. Two more adults in close

contact with infected children have subsequently developed a mild stomatitis which has proved by inoculation of rabbit's corneas to be positive for the virus.

DISCUSSION

These observations indicate that a stomatitis, which is a distinct clinical entity, often accompanied by diarrhea occurs in infants and children. The disease is a moderately severe infection in which symptoms referable to the mouth and intestinal tract predominate. The stomatitis is rather sharply localized to the mucous membranes of the tongue and gums, rarely, if ever, appearing on the palate or mucous surfaces of the cheeks. The reaction is characterized by the appearance of numerous fine vesicles followed by desquamation and superficial ulceration of the epithelium. This is in marked contrast to the definitely local vesiculopapular lesions observed in herpetic stomatitis which are usually distributed over the palate, mucous membranes of the cheeks, and pharyngeal wall as well as the tongue and gums. In about one-third of the children with the presenting symptoms of stomatitis a diarrhea consisting of frequent stools containing much mucus and occasional flecks of blood has been observed. In full-term, newborn infants and especially premature infants a more severe diarrhea is the predominating feature.

The age incidence of the disease is predominately in infants under 6 months of age. It is self limiting in nature and the majority of infants recover within a week or ten days after onset but in many instances the disease has shown a tendency to relapse after periods of improvement. The stomatitis has been observed in two children, 6 and 8 years of age, and on four occasions in adults, three of whom were in close contact with infants with the disease and one who was accidentally infected while working with the virus in the laboratory.

The disease is highly contagious and usually spreads from active cases to susceptible individuals by indirect means. Evidence has been obtained that as a result of close contact with children with the disease adults may become temporary carriers of the virus without developing symptoms or recognizable lesions.

The disease has been found to be caused by a hitherto unrecognized filterable agent. The virus has been successfully propagated in serial passage in the eyes of young rabbits. Swabbings obtained not only from the mouth lesions of infants and children with this type of stomatitis but also from the stools of those with diarrhea due to this agent and inoculated onto the scarified cornea of rabbits produce a reaction which is quite characteristic and can be considered to be diagnostic and indicative of the presence of the virus.

Eyes of rabbits after recovery from infection with the virus of stomatitis and diarrhea of infants develop a specific resistance to reinfection. They do not develop resistance to infection with herpes virus. The character of the microscopic reaction in the corneas of rabbits

and the absence of the intranuclear inclusions in the corneal epithelial cells further differentiates the virus of stomatitis and diarrhea from herpes virus.

Infants with stomatitis, or stomatitis and diarrhea, develop antibodies in their serum which specifically neutralize the virus of stomatitis and diarrhea. An increase in neutralizing antibodies to the virus of herpes does not develop as the result of this disease.

Light and Hodes[3] recently reported the isolation of a filterable agent from the stools of infants during epidemics of diarrhea in nurseries for newborn babies. With the virus they were able to produce diarrhea in calves. There has not been sufficient opportunity to determine whether the virus isolated by Light and Hodes is identical with or differs from the virus isolated in the epidemic of diarrhea in the nursery for newborn infants at Vanderbilt University Hospital. Epidemic diarrhea of the newborn as it usually occurs[4] is a much more acute and severe disease than was the mild infection seen in our nursery.

Observations on this disease and the investigations regarding the nature and behavior of the virus are being continued and await future detailed report.

SUMMARY

1. A stomatitis of infants and children often accompanied by diarrhea is reported. The disease occurs most frequently in infants under 6 months of age.

2. A hitherto unrecognized virus has been isolated from the mouths and from stools of infants with the disease by inoculation of the scarified rabbit cornea. The virus has been propagated and maintained in serial transfer through forty passages in the eyes of young rabbits.

3. The specific causal relation of the virus of stomatitis and diarrhea of infants to the disease has been demonstrated by the appearance of neutralizing antibodies in the convalescent serum of individuals recovering from the condition. Further supportive evidence that this virus is the cause of the stomatitis was obtained from an accidental laboratory infection with filtered material from infected rabbit corneas.

4. The evidence thus far indicates that the virus is highly contagious.

5. The stomatitis has been found to occur sporadically in adults and such persons may serve as sources of infection for susceptible infants. Adults have been found to harbor and spread the virus when they themselves demonstrate no evidence of infection.

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TREATMENT OF INFLUENZAL MENINGITIS WITH SULFADIAZINE

Further Report

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IN OUR preliminary publication (1942)[1] we reported seven cases of influenzal meningitis in children treated at Charity Hospital with five complete recoveries and two deaths. The ages of the patients who recovered were as follows: one, 8 months; one, 15 months; one, 2 years; and two, 3 years. Of these recoveries, three resulted from the use of sulfadiazine alone and two accompanied the administration of this drug and equine anti-influenzal serum. The two fatalities occurred in infants 7 and 5 months old, respectively, the former immediately following a cistern puncture and the latter after a prolonged course complicated by severe infected burns, chicken pox, bilateral mastoiditis, and thrombosis of the lateral sinus.

Since the above report was published, sixteen additional cases of influenzal meningitis in children have been treated at our hospital. These additional cases, together with the seven already reported, serve as the basis of this communication. Inasmuch as complete information regarding our first seven patients appeared in our preliminary publication, the detailed information reported in this paper relates to the sixteen remaining members of our group of twenty-three children with influenzal meningitis.

Case 8.—J. B., a 2-month-old Negro boy weighing 8 pounds (3.6 kg.), was admitted to Charity Hospital Dec. 2, 1942, with a history of fever for one week. Two days before admission he became rigid and developed generalized convulsions. The remainder of the patient's history was irrelevant.

Physical examination on admission revealed marked prostration as well as evidence of severe dehydration. The rectal temperature was 98° F. The anterior fontanel was tense and bulging and the eyes were fixed. Rigidity was present in the neck, body, and extremities, and the Kernig and Brudzinski signs were positive. Examination of the eardrums, heart, and lungs revealed no abnormalities.

The spinal fluid was under a pressure of 280 mm. of water and contained 1,400 leucocytes per cubic millimeter (70 per cent polymorphonuclear cells) and 26 mg. per cent glucose. Type b *Hemophilus influenzae* bacilli were demonstrated on smear and culture. The red blood count was 4 million and the white blood count was 22,000 of which 92 per cent were polymorphonuclear cells.

Therapy consisted of the intravenous administration of 6 grains (0.4 Gm.) of sodium sulfadiazine as an initial dose followed by maintenance doses of 3 grains (0.2 Gm.) every four hours given by stomach tube. Since the patient failed to improve promptly, an additional dose of 13 grains (0.87 Gm.) of sodium sulfa-

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diazine was given intravenously the next day. Unfortunately no anti-influenzal rabbit serum was available in New Orleans at this particular time. The patient died Dec. 4, 1942. Permission for an autopsy could not be obtained.

CASE 9.—L. M. F., a 3-month-old Negro female weighing 8¾ pounds (4 kg.), was admitted Dec. 31, 1941, with a history of an upper respiratory infection of two weeks' duration, drowsiness, and rigidity of the neck for four days, and twitching of the left hand, left foot, and left side of the face for three days.

Physical examination revealed evidence of acute prostration, marked opisthotonos, and drowsiness. The rectal temperature was 102° F. The anterior fontanel was bulging and the neck was rigid. A bilateral myringotomy was done and purulent drainage was obtained from both ears. Decreased breath sounds were heard at the right lung base posteriorly. Spinal puncture on admission revealed a cloudy fluid with 760 leucocytes, 90 per cent being polymorphonuclear cells. *H. influenzae* bacillus type b was isolated on culture.

An initial dose of 12 grains (0.8 Gm.) of sulfadiazine was given orally and this was followed by maintenance doses of 4 grains (0.27 Gm.) every four hours day and night. Anti-influenzal horse serum, 60 c.c., was given intravenously Jan. 1, 1942, and repeated daily for the following four days. The child continued to have generalized convulsive movements and no improvement was noticed. A cisternal puncture Jan. 1, 1942, revealed a purulent fluid. Subsequently the convulsive attacks increased in severity, coma ensued, and the child expired Jan. 6, 1942. An autopsy was not done.

CASE 10.—J. N., a 3-month-old Negro female weighing 8 pounds, 4 ounces (3.0 kg.), entered the hospital Oct. 19, 1942. History was obtained of a draining right ear of three weeks' duration which was associated with high fever until the day of admission. Three days before admission the child's neck became rigid. Twitching of all extremities was noted on the day she entered the hospital.

Physical examination showed the eyes fixed to the right and a purulent discharge from the right ear. The rectal temperature was 102° F. Marked rigidity of the neck was present and the Brudzinski and Kernig reflexes were positive. A cisternal puncture was done because of unsuccessful attempts with spinal punctures. This fluid upon examination showed 2,500 leucocytes (predominantly polymorphonuclear cells), 13.5 mg. per cent glucose; and type b *H. influenzae* bacillus was recovered on culture. The blood showed 3.2 million red blood cells, 7 Gm. hemoglobin (49 per cent), and 25,000 leucocytes of which 88 per cent were polymorphonuclear cells.

Sulfadiazine, 15 grains (1 Gm.), was given intravenously as an initial dose followed by 4 grains (0.27 Gm.) every four hours. Convulsive movements of the extremities were noted Oct. 20, 1942, and the rectal temperature rose to 103° F. Anti-influenzal type b rabbit serum, 50 mg., was given intravenously. The following day bulging of the anterior fontanel became obvious and the child's condition was extremely grave. A ventricular puncture was done and a thick purulent material was withdrawn. Anti-influenzal rabbit serum, 25 mg., was administered into the ventricles at this time and an additional 25 mg. dose was given intravenously. The patient expired Oct. 21, 1942. Permission for a post-mortem examination could not be obtained.

CASE 11.—S. C., a 4-month-old white male weighing 16 pounds (7.6 kg.), was admitted Aug. 25, 1942, because of anorexia, fretfulness, and fever for two days. On the day of admission he developed generalized convulsions and the rectal temperature rose to 104° F. The child was in marked opisthotonos with the head turned to the right, the legs and arms were flexed, and the Kernig and Brudzinski reflexes were positive. The eardrums, heart, and lungs were considered normal.

Since spinal puncture on admission was unsuccessful, a cisternal puncture was done and a thick bloody fibrinous exudate was obtained. On culture, this fluid contained type b *H. influenzae* bacillus. Sodium sulfadiazine, 22 grains (1.5 Gm.), was given intravenously as the initial dose followed by maintenance doses of 4 grains (0.27 Gm.) given orally every four hours. Anti-influenzal rabbit serum was not available at this time.

Spinal puncture Aug. 28, 1942, showed 123 leucocytes per cubic millimeter and *H. influenzae* organisms were still present on culture. The spinal fluid Sept. 3, 1942, contained less than 10 cells per cubic millimeter and the culture was sterile. The temperature dropped to normal Aug. 28, 1942, and subsequently remained normal. The child looked very alert and ate well but continued to hold his head retracted. Sulfadiazine was therefore continued for thirty days, much longer than it should have been. The patient was discharged Oct. 6, 1942, and subsequent examination three months later showed no evidence of residual damage.

CASE 12.—M. R., a 6-month-old Negro male weighing 15 pounds, 4 ounces (6.9 kg.), entered Charity Hospital Nov. 21, 1942. The parents reported that the child had a "cold" and fever for two weeks. For a period of ten days they had noticed a bulging in the region of the anterior fontanel. Physical examination revealed a rigidity of the neck, bulging of the anterior fontanel, slightly exaggerated knee jerks, evidence of prostration, and a purulent discharge from the right ear. The rectal temperature was 101.6° F., and the lungs seemed to be normal.

Spinal puncture on admission resulted in a bloody tap, and smears and culture were both negative. Nevertheless, sulfadiazine, 15 grains (1 Gm.), was given orally as the initial dose followed by maintenance doses of 4 grains (0.27 Gm.) every four hours. The following day the spinal fluid showed 6,200 leucocytes per cubic millimeter with 95 per cent polymorphonuclear cells. The glucose level was 12 mg. per 100 c.c. At this time pleomorphic gram-negative organisms were seen in the spinal fluid smear which on culture proved to be type b *H. influenzae* bacilli.

The rectal temperature had dropped to 99.6° F. on the second day only to rise again to 102° F. Nov. 23, 1942. A continuous drip of 5 per cent dextrose in saline was started and 50 mg. of type specific anti-influenzal rabbit serum and 15 grains (1 Gm.) of sodium sulfadiazine were given intravenously. Intravenous sulfadiazine, 15 grains (1 Gm.), was repeated every twelve hours. On Nov. 24, 1942, the sulfadiazine level in the blood was 13.1 mg. per 100 c.c., and oral sulfadiazine, 7½ (.5 Gm.), every four hours was started. The patient vomited at frequent intervals and the rectal temperature continued to run between 99 and 100° F. On Nov. 27, 1942, the spinal fluid revealed 300 cells but smears and culture were negative. The sulfadiazine blood level had dropped to 2.7 mg. per 100 c.c. Therefore, 15 grains (1 Gm.) were given intravenously and the oral dose was increased to 10 grains (0.67 Gm.) every four hours. The patient gradually became more listless and required gavage feedings. The temperature started to rise, the abdomen became distended, and the child expired Nov. 30, 1942. Consent for an autopsy was refused.

CASE 13.—A. J., an 8-month-old Negro female weighing 16 pounds, 8 ounces (7.5 kg.), was admitted to Charity Hospital Jan. 21, 1943, with a history of having had an upper respiratory infection for three days. On the afternoon of admission the child suddenly became dyspneic. On physical examination the neck was moderately rigid, the eardrums and lungs appeared normal, and Brudzinski and Babinski reflexes were positive. The rectal temperature was 101.2° F. on admission.

Spinal puncture on admission revealed 9,125 cells predominately polymorphonuclear cells. Smear of the fluid showed pleomorphic gram-negative organisms and the culture was positive for type b influenzae bacillus. The red blood count was 4.4 million, the white blood count was 22,800 with 88 per cent polymorphonuclear cells, and the blood culture was negative.

Sulfadiazine, 15 grains (1 Gm.), was given immediately by mouth followed by maintenance doses of 5 grains (0.3 Gm.) every four hours. The child rapidly improved but mild rigidity of the neck continued. The rectal temperature fluctuated between 100 and 102° F. On Jan. 25, 1943, the free sulfadiazine blood level was 11.1 mg. per 100 c.c. and the dosage was increased to 7½ grains (0.5 Gm.) every four hours. On Jan. 25, 1943, the free sulfadiazine spinal fluid level was 7.9 mg. per 100 c.c. On Jan. 29, 1943, the sulfadiazine blood level rose to 13.1 mg. per 100 c.c.

On Feb. 8, 1943, spinal puncture was again repeated. The glucose level was 46 mg. per 100 c.c.; the sulfadiazine level was 6.1 mg. per 100 c.c. and the culture was still positive for *H. influenzae* bacilli. The rectal temperature then began to fluctuate between 101 and 103° F. and the child became weaker and more listless. Anti-influenzal rabbit serum was therefore given on the nineteenth day, 25 mg. intravenously and 25 mg. intraspinally. Within seven days the temperature dropped to normal and the infant appeared much brighter. The red blood count had dropped to 3 million, while the leucocyte count was 15,000. On Feb. 13, 1943, sulfadiazine was reduced to 5 grains (0.33 Gm.) every six hours and finally discontinued Feb. 24, 1943. On Feb. 19, 1943, spinal puncture was normal and culture was sterile. The patient was discharged Feb. 24, 1943, completely recovered. Subsequent checkup two months later revealed no residual damage.

CASE 14.—M. W., a 19-month-old Negro female weighing 22 pounds, 8 ounces (10.2 kg.), entered the hospital Oct. 31, 1942. Her illness dated back to five days prior to admission when she became fretful and restless. Drowsiness developed two days before admission and her neck became rigid. On admission the rectal temperature was 102° F. and the child appeared toxic and lay with the neck in hyperextension. The eardrums, heart, and lungs were essentially normal but the Kernig and Brudzinski reflexes were positive.

Spinal puncture on admission revealed 1,000 leucocytes with 90 per cent polymorphonuclear cells. The smear was negative but the culture was positive for type b influenzae bacillus. Sodium sulfadiazine, 25 grains (1.6 Gm.), was given intravenously as the initial dose followed by oral maintenance doses of 6 grains (0.4 Gm.) every four hours. On Nov. 1, 1942, the temperature dropped to normal. Less rigidity of the neck was noted, and the patient appeared greatly improved. The drug dosage was gradually reduced and discontinued Nov. 17, 1942. The spinal fluid culture Nov. 17, 1942, was sterile. The patient was discharged Nov. 25, 1942, completely recovered.

CASE 15.—S. D., a 19-month-old Negro male weighing 22 pounds (10 kg.), was admitted Nov. 6, 1942, with a history of bronchopneumonia. The patient became increasingly drowsy over a period of five days and was admitted in a stuporous condition. Physical examination revealed an acutely ill child lying in marked opisthotonos. The eardrums, lung fields, and the heart revealed no abnormal findings. The Kernig and Brudzinski reflexes were positive.

Spinal puncture on admission showed 1,500 leucocytes with 90 per cent polymorphonuclear cells, 2+ globulin, and negative culture and smear. Tuberculin tests 1:1,000 and 1:100 were negative. The patient had received 40 grains (2.6 Gm.) sulfanilamide before admission. Sulfadiazine, 30 grains (2 Gm.), was given orally as an initial dose followed by maintenance doses of 6 grains (0.4 Gm.) every four hours. The rectal temperature rapidly dropped to 100° F. on the second day and continued to run between 99 and 100° F. thereafter.

Spinal fluid examination on Nov. 12, 1942, revealed 315 leucocytes per cubic millimeter, chlorides 731 mg. per 100 c.c., and smear and culture were negative.

Repeated small blood transfusions were given. The patient remained in a semi-stuporous condition and feedings were given by stomach tube. On Nov. 16, 1942,

he began having spasmodic generalized convulsions. They were controlled by sodium phenobarbital.

Spinal fluid glucose Nov. 18, 1942, was 45 mg. per 100 c.c. and the blood sulfadiazine level Nov. 20, 1942, was 8.8 mg. per 100 c.c. On Nov. 21, 1942, spinal puncture showed 50 leucocytes per cubic millimeter with 25 per cent polymorphonuclear cells and 75 per cent lymphocytes. The culture was positive for *H. influenzae* type b organism. Anti-influenzal rabbit serum, 50 mg., was given intravenously Nov. 23, 1942. Sulfadiazine, 4 grains (0.3 Gm.), every four hours was continued by mouth and repeated blood transfusions were given as the red blood count was constantly between 2.8 and 3 million cells. The rectal temperature ranged between 99 and 100° F. On Dec. 2, 1942, anti-influenzal rabbit serum, 25 mg. intravenously and 25 mg. intraspinally, was given. The next day the child was still in a semicomatose condition and developed a generalized spasticity of the entire body. Examination of the eye grounds showed no abnormal changes. Spinal puncture was repeated Dec. 16, 1942, and Jan. 4, 1943. Both cultures of spinal fluids were sterile, so sulfadiazine was discontinued. The patient improved very slowly but the generalized spasticity remained. Although there was no block in the spinal canal, attempted encephalogram with 80 c.c. of air was unsuccessful. The patient was discharged with a residual generalized spasticity Jan. 20, 1943.

CASE 16.—O. B., a 2-year-old white boy weighing 29 pounds (13.2 kg.), was admitted to the contagious unit Oct. 13, 1942. Five days before admission the child had developed a severe cough with high fever and chills. A private physician had diagnosed the case as bronchopneumonia. Two days before admission the patient began to hold his head back and the fever remained high. Anorexia developed and vomiting occurred two days before admission. A vesicular rash had appeared on his upper lip three days previously. The only past illness was measles at 1 year of age.

On physical examination, the child was well nourished and well developed but comatose and lying in marked opisthotonos. The rectal temperature was 103° F. and the eardrums appeared normal. Brownish crusts about the nares and herpetic lesions on the upper lip were noted. The neck was rigid. Coarse, scattered râles were heard over the entire lung fields but no definite dullness could be elicited. The heart sounds were normal. The deep reflexes were exaggerated, and the Kernig and Brudzinski reflexes were positive.

Spinal puncture on admission revealed a very cloudy fluid with a cell count of 35,000 leucocytes of which 95 per cent were polymorphonuclear cells. The smear showed gram-negative pleomorphic organisms, and type b *H. influenzae* bacilli were found on culture. The red blood count was 4 million and the white blood count was 16,750.

Sodium sulfadiazine, 60 grains (4 Gm.), was given intravenously initially. Because of the poor condition of the patient it was decided to give all medication intravenously. Sodium sulfadiazine, 10 grains (0.67 Gm.), intravenously was administered every four hours. On Oct. 14, 1942, the spinal tap showed 50,000 leucocytes. The fluid was so purulent that aspiration was necessary. The sugar was 15 mg. per 100 c.c. and chloride 670 mg. per 100 c.c. The culture contained type b *H. influenzae* organisms. Citrated blood, 180 c.c., was then given. Because of the extremely high leucocyte count in the spinal fluid and the low sugar content anti-influenzal rabbit serum, 100 mg., was given intravenously. A continuous drip of 5 per cent glucose in distilled water was started. The patient was still comatose throughout the day. During the night of Oct. 14, 1942, the patient suddenly stopped breathing. Artificial respiration was given until bronchoscopy could be done. A plug of tenacious, sticky, gray material was removed from the trachea. Culture from this material yielded *H. influenzae* bacilli. The child breathed much better, then developed marked dyspnea again. A bronchoscopy and tracheotomy

were then done. The larynx was acutely inflamed and edematous. The trachea was also markedly inflamed and was coated with a grayish, sticky exudate. A croup tent, postural drainage, and 5 per cent carbon dioxide and oxygen inhalations were used at intervals followings the tracheotomy. Because of vomiting all oral fluids and medications were discontinued. On Oct. 15, 1942, the patient's condition remained about the same. Spinal tap on this day again revealed cloudy fluid containing numerous strands of fibrin. Anti-influenzal rabbit serum, 25 mg., was given intraspinally. On the following day, the patient appeared very much improved, although the rectal temperature was still elevated to 102° F. Spinal tap was repeated and revealed the following: 17,600 white blood cells with 82 per cent polymorphonuclear cells; sugar, 18 mg. per 100 c.c.; sulfadiazine level of 46.5 mg. per 100 c.c.; and culture positive for *H. influenzae* bacilli. Blood transfusion of 150 c.c. was given Oct. 15, 1942.

A continuous drip of 5 per cent glucose in distilled water and normal saline was maintained. On Oct. 16, 1942, 300 c.c. of 5 per cent solution of Nutramigen* was given by stomach tube. The next day sulfadiazine was reduced to 15 grains (1 Gm.) every eight hours intravenously. Daily urinalysis revealed numerous crystals but no red blood cells. The patient voided freely throughout this period.

The child continued to improve and began to play with his toys until Oct. 22, 1942. At that time he developed a jerky type of respiration which occurred at irregular periods between which the respiratory efforts were normal. The lung fields were clear and no obstruction could be heard. A bronchoscopic examination revealed no obstruction. The spinal puncture was then repeated and the pressure was found to be 160 mm. of water; cell count, 200 leucocytes; sulfadiazine level, 11.7; sugar, 40 mg. per 100 c.c.; and culture, sterile.

The same type of respiratory difficulty continued the next day. The carbon dioxide combining power was then 78 volume per cent. An infusion of 500 c.c. lactate-Ringer's solution was given followed by normal saline. Within four hours the respiration became normal. On Oct. 21, 1942, the continuous infusion was discontinued.

Sulfadiazine was continued by mouth in decreased dosage. The tracheotomy tube was removed Nov. 6, 1942. On Nov. 13, 1942, sulfadiazine was discontinued. Spinal puncture revealed clear spinal fluid, the cell count was less than 10 cells, the sugar was 50 mg. per 100 c.c. and the culture was sterile. He was discharged Nov. 24, 1942, afebrile and with no apparent residual damage. A follow-up six months later revealed no residual damage.

CASE 17.—S. W., a 2-year-old Negro female weighing 22 pounds (10 kg.), entered the hospital Jan. 25, 1943, with a history of an upper respiratory infection with fever which began three days before admission. The child became increasingly lethargic over this period of time. On the morning of admission she developed generalized convulsions and the rectal temperature was 102° F. Examination revealed normal eardrums, moderate inflammation of the pharynx, slight rigidity of the neck, normal heart and lungs, and positive Kernig and Brudzinski reflexes. The spinal fluid contained 225 leucocytes predominately polymorphonuclear cells. The sugar was 69 mg. per 100 c.c. and type b influenzal organisms were found on culture.

Sodium sulfadiazine, 45 grains (3 Gm.), was given intravenously followed by 5 grains (0.3 Gm.) every four hours orally. Although the child appeared much better two days later, the temperature was still elevated to 102° F. rectally. Consequently anti-influenzal rabbit serum, 35 mg., was given intravenously. On Jan. 28, 1943, the neck was no longer rigid. At this time the patient developed a gross hematuria after a total of 130 grains (8.67 Gm.) of sulfadiazine had been given. The drug was stopped and fluids were forced. On Jan. 29, 1943, the tem-

*Mead Johnson & Co., Evansville Ind.

perature had dropped to normal. The spinal fluid on this date contained 46 cells and the culture was sterile. The patient remained afebrile and was discharged one week later completely recovered.

CASE 18.—M. E., a 2½-year-old Negro female weighing 28½ pounds, entered Charity Hospital June 28, 1942, with a history of fever and anorexia for three days and hyperextension of the neck for one day. On physical examination the child was fairly alert with the head drawn back and both thighs flexed. The eardrums, heart, and lungs were normal and Brudzinski and Kernig reflexes were positive. Spinal puncture on admission showed the fluid to contain 500 leucocytes per cubic millimeter with 76 per cent polymorphonuclear cells and 24 per cent lymphocytes. The sugar was 35 mg. per 100 c.c. and the hemoglobin was 80 per cent. The red blood count was 4.5 million and the white blood count was 9,600. Culture of the spinal fluid was positive for *H. influenzae* bacilli.

An initial dose of sulfadiazine, 45 grains (3 Gm.), was given orally followed by maintenance doses of 15 grains (1 Gm.) every four hours. The maintenance doses were continued until July 5, 1942, when the dose was reduced to 10 grains (0.67 Gm.) every four hours. On July 8, 1942, it was further reduced to 5 grains (0.33 Gm.) every four hours and remained at this dose until it was discontinued July 18, 1942.

On June 28, 1942, 50 mg. of anti-influenzal type b rabbit serum were given intravenously. The temperature dropped to normal July 3, 1942. Sulfadiazine blood level July 3, 1942, was 11.7 mg. Spinal puncture done July 27, 1942, was sterile. The patient was discharged Aug. 2, 1942, completely recovered.

CASE 19.—O. H., a 2-year-old Negro male weighing 33 pounds (15 kg.), was admitted June 11, 1942, with a history of headache and fever which began five days prior to admission. On admission the rectal temperature was 101.8° F. The child lay quietly on his side with the lower extremities in flexion and the neck moderately rigid. The eardrums, heart, and lungs were normal.

A spinal puncture on admission revealed a pressure of 240 mm. of water. The fluid contained 3,540 leucocytes, predominately polymorphonuclear cells. No organisms were seen on direct smear. The culture, however, was positive for *H. influenzae* type b bacilli.

Sulfadiazine, 30 grains (2 Gm.), was given orally followed by 10 grains (0.67 Gm.) every six hours. On June 26, 1942, the culture of the spinal fluid was sterile. Sulfadiazine was discontinued July 4, 1942, and the patient was discharged July 10, 1942, completely recovered.

CASE 20.—W. L., a 2-year-old white female weighing 35 pounds (15.8 kg.), entered the hospital June 23, 1942. History was obtained of fever and vomiting for one day. The rectal temperature on admission was 103.6° F. The child appeared apprehensive and responded poorly to questioning. The eardrums appeared normal, the neck was rigid and painful to movement, and respirations were rapid although no râles were heard. The Kernig and Brudzinski reflexes were positive. Roentgenogram of the chest showed bronchopneumonia at both bases.

Spinal puncture on admission revealed 2,500 cells, predominately polymorphonuclear cells. Type b *H. influenzae* organisms were found on culture of the spinal fluid. Sulfadiazine, 30 grains (2 Gm.), was administered intravenously as the initial dose. This was repeated in two hours. The drug was then administered orally, 10 grains (0.67), every four hours. Anti-influenzal rabbit serum, 75 mg., was given intravenously on the day of admission. On June 25, 1942, the temperature was normal. Sulfadiazine was gradually reduced and discontinued July 11, 1942. The patient was discharged July 18, 1942.

CASE 21.—E. D., a 4-year-old Negro female weighing 31 pounds (14.1 kg.), was admitted June 11, 1942, with a history of fever, anorexia, and rigidity of neck

for four days. Physical examination revealed an acutely ill, lethargic child with the head hyperextended, the back arched backward, and the knees flexed on the abdomen. The rectal temperature was 101.8° F. The eardrums, throat, heart, and lungs were normal. Kernig and Brudzinski reflexes were markedly positive. Spinal fluid examination on admission revealed a pressure of 300 mm. of water, 5,320 cells with 79 per cent polymorphonuclear cells. Type b influenzal organisms were found on culture and direct typing.

Sulfadiazine, 45 grains (3 Gm.), was given intravenously as the initial dose followed by 7½ grains (0.5 Gm.) orally every four hours. Anti-influenzal rabbit serum, 25 mg., was given intravenously on the day of admission. On June 13, 1942, the patient was afebrile. The sulfadiazine blood level on this day was only 3.8 mg. per 100 c.c. On June 16, 1942, spinal fluid examination showed less than 10 cells per cubic millimeter, sugar 43 mg. per 100 c.c., and the culture was sterile. On June 17, 1942, the sulfadiazine level was 8.9 mg. per 100 c.c. Sulfadiazine was gradually reduced and discontinued June 20, 1942. The patient was discharged without any apparent residual damage June 27, 1942.

CASE 22.—K. B. L., a 6-year-old Negro female weighing 54 pounds (24.5 kg.), was admitted to the hospital Oct. 19, 1943, with a history of coryza and fever for two days. On the day of admission she began to vomit and complain of a severe headache. On physical examination we noted a well-developed, well-nourished female, very toxic and extremely irritable. The rectal temperature was 103.8° F. The head was held in hyperextension. The eardrums, lungs, and heart were normal and Kernig and Brudzinski reflexes were markedly positive. Spinal puncture on admission revealed the following: Pressure, 410 millimeters of water; 17,500 cells with 98 per cent polymorphonuclear cells; sugar, 33 mg. per 100 c.c. of spinal fluid. Type b *H. influenzae* bacilli were found on culture.

Sodium sulfadiazine, 40 grains (2.67 Gm.), was given intravenously and 10 grains (0.67 Gm.) every four hours orally. On Oct. 22, 1943, the sulfadiazine blood level was 7.9 mg. per 100 c.c. so the drug was increased to 15 grains (1 Gm.) every four hours. On Oct. 23, 1943, the temperature was normal. The dosage of sulfadiazine was reduced Oct. 29, 1943, to 7½ grains (0.5 Gm.) every four hours. On Nov. 8, 1943, the rectal temperature again rose to from 101 to 103° F. and continued at this level until sulfadiazine was discontinued Nov. 11, 1943. Within forty-eight hours after the drug was discontinued, the temperature was normal and remained so until discharge. Only one spinal puncture was done (on admission).

CASE 23.—W. S., a 7-year-old Negro male weighing 45 pounds (20.4 kg.), was admitted to the hospital May 21, 1942. He gave a history of fever and headache for six days. Three days before admission his neck became rigid. At the time of admission the rectal temperature was 102° F. He appeared acutely ill and lay in opisthotonos. The examination of the ears, throat, heart, and lungs revealed no abnormalities. Kernig and Brudzinski reflexes were positive.

Spinal puncture revealed a cloudy fluid containing 1,800 cells, predominately polymorphonuclear cells. The sugar was 33 mg. per 100 c.c. of fluid. The smear was negative, but the culture revealed type b *H. influenzae* organisms. The blood culture was negative. Sulfadiazine, 30 grains (2 Gm.), was given orally as the initial dose followed by 15 grains (1 Gm.) every four hours. The sulfadiazine blood level was 4.7 mg. per 100 c.c. May 23, 1942. The patient became afebrile by the end of the third day. The dosage of sulfadiazine was reduced May 26, 1942, and discontinued May 29, 1942. The patient was discharged June 2, 1942, completely recovered.

A summary of the 23 patients with influenzal meningitis treated with sulfadiazine at Charity Hospital during the past two years is given in Table I.

TABLE I

SUMMARY OF AVAILABLE DATA ON TWENTY-THREE PATIENTS WITH INFLUENZAL MENI

PATIENT, SEX, AGE, RACE	WEIGHT (POUNDS)	SULFADIAZINE				FREE DRUG LEVEL		DA DIS TREA BE
		INITIAL DOSE (GRAINS)	MAINTENANCE DOSE		TOTAL DOSE (GRAINS)	BLOOD (MG./100 C.C.)	SPINAL FLUID (MG./100 C.C.)	
			GRAINS PER POUND DAILY	DAYS GIVEN				
G. B., ♂, 2 mo., Negro	8	6	2 to 3	2	3	--	--	8th
L. M., ♀, 3 mo., Negro	8¾	12	3	6	13	--	--	5th
J. N., ♀, 3 mo., Negro	8¼	15	3	2	3.3	--	--	4th
S. G., ♂, 4 mo., white	16	22	1½	30	48	--	--	3rd
M. L., ♀, 5 mo., Negro	11	11	2½ to 2	30	48	20.7	9.7	3rd
M. R., ♂, 6 mo., Negro	15	12	2 to 4	9½	25.6	13.1 2.7	--	11th
C. K., ♀, 7 mo., Negro	14½	15	2	1	15	--	--	4th
C. G., ♂, 8 mo., Negro	18	18	2	19	46	--	--	3rd
A. J., ♀, 8 mo., Negro	16½	15	2	24	72.6	11.1 9.5 13.1 6.1	6.1	4th
C. J., ♂, 15 mo., Negro	18	18	1½ to 1 to ½	24	36	25	15	3rd
M. W., ♀, 19 mo., Negro	22½	25	1½	18	28½	6.4	--	6th
S. D., ♂, 19 mo., Negro	22	30	1¾ to 1½	58	141.2	8.8	--	6th
B. W., ♀, 2 yr., Negro	30	22½	2 to 1	26	92	19.3 to 25	10	2nd
O. B., ♂, 2 yr., white	29	60	2	32	84	--	46.5 11.7	3rd
S. W., ♀, 2 yr., Negro	22	45	2 to 1½	4	10	--	--	4th
M. E., ♀, 2½ yr., Negro	28	45	3	20	80	--	11.7	4th
O. H., ♂, 3 yr., Negro	33	30	2	24	72.6	--	--	6th
W. L., ♀, 3 yr., white	35	30	1¾	19	67	6.7	--	2nd
B. B., ♀, 3 yr., white	37	30	2 to 1½	19	80	17	11	1st
R. S., ♂, 3 yr., white	30	30	1 to ½ to ⅓ to ¼	19	28	13.8	--	1st
E. D., ♀, 4 yr., Negro	31	45	1	19	50	3.8 8.9	--	5th
K. L. B., ♀, 6 yr., Negro	54	40	2 to 1½	25	86	7.9	--	1st
W. S., ♂, 7 yr., Negro	45	30	1½	8	75	4.7	--	4th

TABLE I

MENINGITIS TREATED WITH SULFADIAZINE AT CHARITY HOSPITAL

DAY OF DISEASE TREATMENT BEGAN	TOTAL ANTISERUM GIVEN	SPINAL FLUID CULTURE	DAYS OF TEMPERATURE ELEVATION IN HOSPITAL	SPINAL TAPS (NO.)	COMMENT
8th day	Unable to obtain serum	?	Temperature subnormal	1	Patient expired; block
5th day	Horse serum, 300 c.c.	?	7	2	Patient expired
4th day	Rabbit serum, 100 mg.	?	2	2	Patient expired; block
3rd day	----	Negative, 9th day	3	4	Complete recovery
3rd day	----	Negative, 5th day; positive 22nd	7	3	Complicated by burn, chicken pox; premature cessation of therapy; relapse; death
11th day	Rabbit serum, 50 mg.	?	9½	3	Persistent vomiting; patient expired
4th day	Horse serum, 300 c.c.	?	1	4	Patient expired during cisternal tap
3rd day	Horse serum, 270 c.c.	Positive, 12th day; negative 23rd day	11	3	Complete recovery
4th day	Rabbit serum, 50 mg.	Negative, 29th day	26	5	Complete recovery
3rd day	----	Negative, 3rd day	8	3	Complete recovery
6th day	----	Negative, 18th day	2	2	Complete recovery
6th day	Rabbit serum, 100 mg.	Negative, 40th day	62	8	Residual generalized spasticity
2nd day	Horse serum, 60 c.c.	Negative, 8th day	19	4	Complete recovery
3rd day	Rabbit serum, 100 mg.	Negative, 10th day	13	6	Tracheobronchitis; tracheotomy; complete recovery
4th day	----	Negative, 4th day	4	2	Complete recovery; gross hematuria
4th day	Rabbit serum, 50 mg.	Negative, 30th day	5	2	Complete recovery
6th day	----	Negative, 15th day	11	2	Complete recovery
2nd day	----	?	8	1	Complete recovery
1st day	----	Negative, 7th day	3	2	Complete recovery
1st day	----	Negative, 4th day	9	2	Complete recovery
5th day	----	Negative, 5th day	2	2	Complete recovery
1st day	----	?	4	1	Drug fever; complete recovery
4th day	----	?	2	1	Complete recovery

COMMENT

A glance at the summary, Table I, will show that six deaths occurred out of a total of twenty-three cases making a mortality of 26 per cent. This is a remarkable improvement over that of previous years when the mortality at Charity Hospital totaled nearly 100 per cent (Aleman,[2] Tripoli).[3] The reduction in mortality can be traced to two factors: chemotherapy with sulfadiazine and serotherapy. Further analysis of data shows that the mortality is confined to infants below 8 months of age. Out of seven cases in this group only one recovery occurred. All children above 7 months of age recovered, one with residual generalized spasticity, the others without any residuals. This finding is in accord with Alexander's statements[4] that infants below 7 months of age with influenzal meningitis have a far higher mortality than above this age.

Three factors appear to contribute to poor prognosis in young infants: the first is the development of early block in the cerebrospinal system; the second is the tendency to late diagnosis or misdiagnosis of the disease and hence delayed therapy; and the third might be lack of resistance in these patients. Moreover, in these young patients drug administration orally or intravenously is much more difficult than in older children, and since blood levels are not as closely followed because of the difficulty of venipuncture, the drug level in the blood and spinal fluid is often allowed to become extremely low. The frequency of vomiting, dehydration, and acidosis further complicates therapy and may contribute to the higher mortality.

One patient, 19 months old, developed a residual generalized spasticity. We marvel that more patients do not develop residual generalized spasticity when in the fatal cases pathologists see so much thick fibrinous pus over the base of the brain and often throughout the ventricles.

We regret that laboratory studies are not as complete or as adequate as they should have been, but wartime has placed a severe strain on personnel in our hospital, as it has in all others. Both chemotherapy and serotherapy could have been more promptly and adequately administered if conditions had been more favorable.

Our previous experiences with the old horse serum have convinced us that this form of therapy is of very little value. We therefore attribute the recovery of patients receiving this serum to sulfadiazine rather than to the equine antiserum. It is significant that the only infant below 8 months of age who recovered received no serum. Success must of necessity be credited to chemotherapy.

We do not feel that the new type-specific anti-influenzal rabbit serum has been given a fair trial in our series. Often this serum was not available in the city. At other times a sufficient amount could not be obtained. Our observation, after a limited experience, seems to suggest that rabbit serum gives much more prompt response and improvement when used together with sulfadiazine. It is our impression that

the cerebrospinal fluid is sterilized much more rapidly when type-specific serotherapy is combined with drug therapy.

Of sixteen patients 8 months old or above, all of whom recovered, four patients received rabbit anti-serum and two patients equine serum. All others received sulfadiazine alone. The patient with residual spasticity received rabbit serum rather late, after he failed to give adequate response to sulfadiazine.

Unquestionably, the ideal treatment would be a combined therapy using rabbit serum in maximal dosage and sulfadiazine. The results we obtained in our series seem to suggest to us that all young infants below 8 months of age should invariably receive the combined therapy. In view of our high mortality in these young infants, prompt therapy is imperative. To accomplish this, it is suggested that rabbit antiserum in maximal dosage of 100 mg. or more be promptly administered if immediate smears from the spinal fluid reveal doubtful or no organisms.

Since all our cases were type b influenzal cases, it appears that direct typing may not be a necessary requirement before administering the type-specific sera.

Sulfadiazine blood and spinal fluid levels were not closely followed, so we are unable to say what the optimal level for recovery may be. Even if this were closely followed, it would be a difficult matter to settle the question of optimal level.

Very few complications were encountered with the administration of sulfadiazine in spite of the large doses used. One patient developed leucopenia; one, a drug fever; and one, gross hematuria. All of these toxic symptoms rapidly disappeared with discontinuance of the drug. No kidney blockage was encountered.

The case of O.B., a two-year-old white male, who also had a severe influenzal tracheobronchitis which necessitated a tracheotomy, is truly remarkable. His spinal fluid was so thick and purulent that drainage would not occur unless aspirated. Moreover, a free sulfadiazine level of 46.5 mg. per cent (checked twice) in the spinal fluid without any evidence of kidney irritation or blockage is worthy of note. This high level was obtained unintentionally and certainly was probably unnecessary. Anyone seeing this patient would have given him up as a certain fatality. We were resigned to this fact. A complete recovery makes the case even more remarkable.

Other unpublished data indicate to us that the initial dose of sulfadiazine should best be given intravenously since excretion into the cerebrospinal fluid occurs more promptly and in higher concentration than when orally administered. It is also our impression that high blood and spinal fluid levels early in the course of therapy are far more efficacious than low levels early followed by high levels later. Above all, early combined chemotherapy and type-specific serotherapy seem to be the most efficacious treatment of influenzal meningitis.

SUMMARY

Twenty-three children with influenzal meningitis have been treated at the Charity Hospital in the past two years with sulfadiazine. Sixteen patients have been discharged as cured and have remained well except one patient who developed and still has a residual generalized spasticity. Six fatalities occurred, all in young infants below 8 months of age. In this group only one recovery occurred in an infant 4 months old. In our series no fatalities occurred above the age of 8 months. Since sulfadiazine alone does not seem sufficient in these young infants, it is imperative that type-specific rabbit antiserum be given together with large doses of sulfadiazine.

In older infants and children the recovery rate is very high with sulfadiazine alone.

Very few spinal punctures and drainages were performed.

Leucopenia in one patient, hematuria in one patient, and drug fever in one patient were the only toxic conditions encountered that can be attributed to the drug.

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EXPERIENCES WITH A CONVENIENT METHOD FOR CULTURING STOOLS

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THE chief purposes of this communication are to call attention to a convenient method for culturing stools and to illustrate the value and feasibility of using this special diagnostic procedure routinely on children admitted to hospitals as well as on all patients who develop diarrhea while on the ward. The method to which we refer was brought to our attention by Dr. James Watt, of the United States Public Health Service, during the course of the special study of dysentery he was conducting at Charity Hospital in New Orleans. A description of this procedure has been published by Hardy, Watt, and Decapito.[1]

Ordinarily, stools are collected by parents, nurses, or other attendants who deliver or send the specimens to the laboratory where they are subsequently cultured. The delays that often attend this procedure materially diminish its reliability owing to the fact that the efficiency of bacteriologic examinations of stools is contingent to a considerable degree on culturing fecal material promptly after defecation and before nonpathogenic organisms have had sufficient time to proliferate appreciably in the specimen.[2-4]

As compared with this procedure, the convenient method of culturing stools being used on our service has several advantages. It enables one to obtain single or repeated cultures of fresh fecal material promptly at the time of admission as well as following the development of diarrhea subsequent to admission. It obviates the necessity of waiting for defecation to occur and does not require the collection of stools. Furthermore the convenient method permits one to start the culture during hours when the laboratory is closed. Apparently its efficiency is essentially on a par with that of other methods used commonly for obtaining stool cultures.[2] In our convenient method of culturing stools, a small pledget of dry sterile cotton, which has been wrapped tightly around one end of an ordinary wood applicator, is inserted directly into the infant's rectum for a distance of 5 or 6 cm. The fecal material is collected on the cotton by rotating the swab in such a manner as to cause it to sweep gently into different parts of the lumen of the rectum. After the swab is withdrawn the fecal specimen is immediately smeared over practically the entire surface of a Shigella-Salmonella agar plate.* This medium has been found by Butterfield and Burns,[1a] Hardy, Watt, and Decapito,[1] and Cooper, Keller and

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*SS agar, Difco Laboratories, Inc., Detroit, Mich.

Glesne[5] to be very satisfactory for culturing stools. It permits the proliferation of shigellae, salmonellae, and eberthellae but inhibits the multiplication of nonpathogenic organisms. After incubating the culture, appropriate procedures are used to identify the organism recovered from the stool.

When dealing with patients beyond the age of infancy, voluntary contraction of the anal sphincter usually interferes with the insertion of the dry cotton pledget and makes the procedure painful. This difficulty is overcome by using a piece of rubber tubing which is long enough to enclose about two-thirds of the length of the applicator and through which the swab passes with ease. After lubricating the beveled end of the tubing without contaminating the cotton pledget which it protects, the unit is inserted into the rectum a distance of 5 or 6 cm.

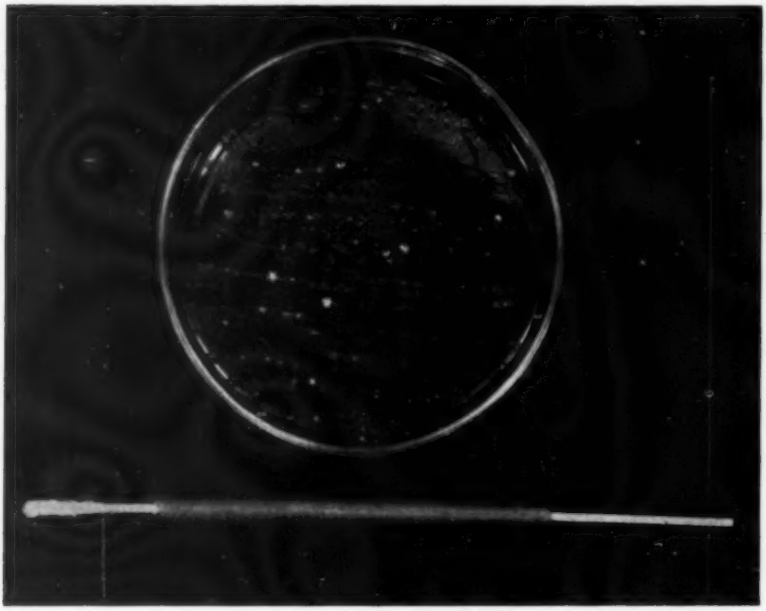

Fig. 1.—A twenty-four-hour culture and equipment used in obtaining it.

The cotton swab is then exposed by withdrawing the tube approximately 3 cm. along the shaft of the applicator and the fecal specimen is collected. Finally the swab is drawn back into the tube and the entire unit is removed from the rectum. Throughout this procedure it is advisable to compress the rubber tubing between the fingers in order to prevent undesired discharges of fecal material. The equipment needed for this simplified method of culturing stools and one of the cultures obtained through its use are illustrated in Fig. 1.

The method we have described probably is the best single procedure available for culturing stools routinely, but under special circumstances more elaborate techniques should be used. Fecal specimens obtained by rectal swab are not suitable for demonstrating ova, cysts, and parasites.

With the cooperation of Dr. James Watt and his technician, Miss Elizabeth Carlton, the culturing of stools by this convenient method has been done routinely since May, 1943, on all children under our care regardless of the causes for their admission to the hospital. As a matter of convenience, a supply of sterile swabs and Shigella-Salmonella agar plates was maintained at the central service station on the pediatric floor. The stool cultures were made on all patients shortly after their admission to the ward. When the program had been in operation a short time, it became obvious that culturing stools with the convenient technique we were using was easier and less time consuming than culturing the throats of rebellious infants and children. It also became obvious that the scope of a program for making routine stool cultures is determined by the number of cultures a technician can examine completely rather than by the number of cultures that can be taken per day. The service of one full-time technician was more than adequate for this study.

The routine culturing of stools yielded instructive and orienting results. Various types of pathogenic bacteria which commonly cause diarrhea were recovered from the stools of some patients who presented no gastrointestinal symptoms. They were also recovered from afebrile children whose extremely mild symptoms consisted in having from two to three unformed yellow stools per day which contained no macroscopic blood or pus and could hardly be considered diarrheal in character. Cases of this type were found with sufficient frequency to give us the impression that the incidence of mild dysentery infections may be distinctly higher in children than is generally appreciated. The survey also disclosed evidence which indicated the occasional occurrence of cross-infections in the wards. A few selected experiences are reported in this communication.

After our program had been in operation a few weeks a 3-year-old Negro female who had had a fever for five days was admitted to the hospital. There was no history of antecedent vomiting or diarrhea and no other member of the family was ill. The child's examination was negative except for a rectal temperature of 105.4° F. and the presence of a few moist râles over the chest. In view of these findings a tentative diagnosis of bronchopneumonia was made and sulfadiazine was prescribed. Forty-eight hours later *Eberthella typhi* was identified in the stool culture that had been taken routinely on admission. The patient was immediately removed from the general pediatric ward. Her temperature remained elevated for an additional six days and the stool cultures were positive for a total of two weeks. Before the pa-

tient left the hospital her agglutination titer for *E. typhi* was 1 to 640. In this instance the program of culturing stools routinely resulted in the prompt detection of unsuspected typhoid fever, a comparatively rare disease in infants.

The cases we have seen occasionally in which infection with organisms belonging to the dysentery group failed to cause diarrhea and vomiting can be illustrated by our experience with a 16-month-old Negro male who had ingested lye a few hours prior to his admission to the hospital. The routine culture taken shortly after the patient entered the ward yielded Flexner dysentery bacilli which continued to be present in his stools for three successive days and then disappeared in response, apparently, to sulfonamide therapy. This patient had no gastrointestinal symptoms prior to the time he ingested lye and he did not develop diarrhea during his protracted period of hospitalization.

In several instances the diarrhea, vomiting, and general symptoms that accompanied the presence of dysentery bacilli in the stools were very mild and transient. An occasional child was also seen whose dysentery infection produced several general manifestations of illness but failed to cause gastrointestinal symptoms of importance. For example, a 10-month-old Negro male was admitted to the hospital because of fever of two days' duration. The initial examination revealed a pronounced generalized hypertonicity of muscles, a rectal temperature of 106° F., a normal spinal fluid, and a white blood cell count of 23,600, of which 43 per cent were polymorphonuclear leucocytes. In addition, the blood culture was negative on one occasion. There was no history of antecedent diarrhea. The child had one watery stool shortly after entering the ward, and subsequently only two or three soft yellow stools were passed daily. The routine stool culture disclosed *Shigella sonnei* which remained present in the stool for three days. The rectal temperature fluctuated between 100 and 102° F. over a period of sixteen days, and the hypertonicity of muscles persisted for three weeks. The child's recovery was complete. In this case gastrointestinal symptoms were trivial as compared with the other manifestations of illness.

The value of routine stool culture in revealing the probable explanation of severe symptoms whose etiology might otherwise escape identification can be illustrated by our experience with a 2½-day-old white male who was brought to the hospital because of a high fever of fourteen hours' duration and a generalized convulsion. The baby had received a formula of evaporated milk but had had no diarrhea or vomiting. Owing to the negative physical findings and the normal spinal fluid and urine, no explanation was found for the infant's temperature of 104° F. and the severe manifestations of illness. Twelve hours after admission the baby passed a soft yellow stool which could hardly be classed as diarrheal. This extremely mild gastrointestinal

manifestation persisted for forty-eight hours, and two days later the infant's temperature was normal. The culture taken on admission, and thus prior to the appearance of yellow stools which totaled four per twenty-four hours, was positive for *Salmonella typhi murium*. Except for this finding no plausible explanation for this infant's illness was discovered. The stools were still positive when the infant was discharged at the end of thirteen days of hospitalization. One month later the culture was negative.

The results of routine stool cultures have led us to question the validity of some of our preliminary diagnoses which attributed gastrointestinal symptoms to parenteral infections. For example, a 10-month-old Negro female was admitted to the hospital because of fever and vomiting over a period of eight hours. There was no history of diarrhea, and during the period of hospitalization the stools were normal. The initial examination revealed a rectal temperature of 102° F. and a purulent discharge from the right ear. Tentatively the patient's fever and vomiting were attributed solely to otitis media. Eight hours later Flexner dysentery bacilli were found in the routine stool culture taken on admission to the hospital. Whether this child's vomiting was secondary to otitis media or was caused by the dysentery organisms is problematical. Comparable experiences with other patients have rendered it difficult to determine with certainty whether the gastrointestinal symptoms were secondary to parenteral disease or were caused by the pathogenic bacteria recovered from the stools.

The evidence we disclosed which indicated the occurrence of cross-infection in the wards is exemplified by the record of an 8-month-old Negro male who was admitted to the hospital because of a cough and fever of two days' duration. The initial examination revealed a rectal temperature of 103° F. and fine râles throughout both lungs. A tentative diagnosis of bilateral bronchopneumonia was made and sulfadiazine was prescribed. Subsequent examination confirmed this diagnosis. The routine stool culture taken the day the patient entered the ward was negative. After a period of severe illness the temperature began to subside and returned to normal the tenth day following the child's admission to the hospital. Six days later the fever recurred and the patient developed loose green stools from which Salmonella Newport was recovered. The same type of organism had been demonstrated in the stools of another patient with diarrhea who entered the ward a few days prior to the onset of diarrhea in the child who was convalescing from pneumonia. Evidence of additional cross-infections in the wards has been disclosed. These will be reported in a later publication by Dr. Watt.

Recently we have been making stool cultures on selected patients in the outpatient department. This experience combined with that gained in the ward has convinced us that the convenience of the method we are employing for culturing stools makes this diagnostic procedure

practical for use by physicians in their office, home, and hospital practice. The culture medium is readily prepared by adding the dehydrated SS agar to cold water and bringing the solution to a boil. The preparation is then poured into sterile Petri dishes and is ready for use when solidified. After the culture has been taken, it may be delivered later in the day to the laboratory for incubation and study.

SUMMARY

This communication calls attention to a convenient method which enables one to obtain cultures of fresh fecal material without having to wait for defecation to occur and also obviates the necessity of sending stools to the laboratory for examination. Its efficiency has been reported to be essentially equal to that of the less convenient procedures used commonly for culturing stools, and its simplicity and ease of performance places stool culturing practically on a par with throat culturing.

Our program of culturing stools routinely with this convenient method resulted in the prompt diagnosis of typhoid fever in one infant and disclosed several instances in which gastrointestinal symptoms either failed to accompany the presence of pathogenic organisms in the stools or were extremely mild and transient. The program also revealed dysentery infection in children whose gastrointestinal symptoms had been attributed tentatively to parenteral disease and demonstrated the occurrence of an occasional cross-infection in the wards.

Our experience has convinced us that physicians will find this simple and convenient method for culturing stools suitable for use in their office, home, and hospital practices.

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THE TREATMENT OF HYPERTHYROIDISM IN CHILDREN

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SINCE 1922, when iodine was introduced into the preoperative treatment of hyperthyroidism, there has been very little argument against treating all patients with toxic goiter by operation. Before this time the operative mortality rate in children was nearly 10 per cent, but with the judicious use of iodine it has since dropped to a respectable 2½ per cent. In recent years, however, a few clinicians have again been questioning whether surgical removal is the best treatment for all cases of hyperthyroidism occurring in children. It is always desirable to avoid surgery if the patient can be treated successfully by medical means alone, and there is an increasing number of reports testifying to the fact that more and more children are enjoying permanent arrest of their toxic symptoms without surgery. It is the purpose of this report to add four more cases to that list and to discuss the means of treatment, other than surgery, of thyrotoxicosis in childhood.

REVIEW OF THE LITERATURE

There have been few comprehensive reports written about the treatment of toxic goiter in childhood. In 1926 Helmholz[1] reported a series of children seen at the Mayo clinic over the five-year period from 1921 to 1926. This series consisted of thirty patients, all under 14 years of age. Four were boys and twenty-six were girls. Of these, twenty-four were operated on. Two died during their postoperative course, one of pneumonia and the other during a thyroid crisis. Three of the children did not remain for treatment. The remaining three made complete recoveries under conservative management. The Crile clinic[2] in Cleveland reported in 1927 that the operative mortality rate there had been no higher in children than in adults. Of fifty-four children operated on, two deaths occurred. Crile gave the case reports of four children under 5 years of age. Three recovered following thyroidectomy and the other was treated successfully by conservative therapy. Crile's conclusion was: "Although our experience with conservative therapy has not been satisfactory and we have rarely been able to control the disease without operation, in mild or early cases when the patient can be kept under close observation conservative measures can safely be given a trial."

In a more recent article, 1940, Reilly, of the University of California Medical School,[3] presented an analysis of the natural course of the disease in childhood and of the relative merits of the surgical and non-

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surgical treatment. The report was based on observations of sixty-two patients over a twenty-five-year period. Reilly found that the disease is most common between the twelfth and fourteenth years and is usually arrested by the eighteenth year. Medical therapy was tried on thirty patients before surgery was resorted to. Fifteen of these were successfully treated by conservative measures, the treatment usually requiring from three to six months but in some cases from ten to twelve months. For the other fifteen children medical therapy failed and either surgery or roentgen ray treatment was used. In this series of patients roentgen therapy was used mainly as a supplement to surgery, preoperatively or in recurrences, but it was used without surgery for five patients. Complete arrest of symptoms was accomplished in four of these and marked improvement occurred in the fifth. Surgery was successful in 90 per cent of the cases in which it was used. There were recurrences in 6 per cent, permanent hypothyroidism in three patients, and permanent hypoparathyroidism in two patients. Reilly stated that: "It might be deduced that in half of the cases thyroid hyperplasia is relatively benign, self-limited, short lived, and not a great menace to health in childhood or in later life."

REVIEW OF PATIENTS TREATED AT THE UNIVERSITY HOSPITAL

Because of the recent controversy and the lack of convincing evidence in the textbooks and literature regarding the treatment of exophthalmic goiter in children, it was decided to review the records of all the children with this disease who have been treated at the University Hospital. Between 1925 and 1943 twenty-three patients were treated. All the children were girls and their ages ranged from 7 to 16 years. Of these patients nineteen were operated on and four were treated by conservative therapy alone. An effort was made to obtain a report of the present condition of each of the patients. All but six of them sent in detailed accounts of their progress since their last visit to the hospital. These six children had all been operated on and are listed in the following statistics according to the amount of improvement noted at their most recent visit to the hospital. As nearly as could be determined, nine of the nineteen patients operated on obtained complete and lasting relief of symptoms. Three more stated that for the most part they were well but still complained of minimal nervousness and fatigue. Five of the children operated on had a definite return of symptoms within a short time after their operations. Two of these returned to the hospital and were subsequently given complete relief, one by reoperation and the other by roentgen therapy. The other three patients have not as yet returned for further treatment and still have their symptoms. The remaining two patients on whom operations were performed are listed as operative mortalities. Both died in thyroid crises a few hours after operation. Both had unusually severe symptoms and

some degree of cardiac enlargement before operation. They had been little benefited by the ordinary short period of preoperative preparation. No serious complications occurred in any of the patients operated on who survived. There is no indication that any of them later developed signs of hypothyroidism, hypoparathyroidism, or other deficiency which could be related to operation. Excluding two children who were kept an unusually long time for metabolic studies, the average period of hospitalization for those in the operated group was thirty-five days. With only two or three exceptions, treatment was discontinued at the time of discharge and the patient was allowed full activity within a short time after returning home. The total period of treatment for the patients operated on, then, may be considered as slightly longer than the period of hospitalization.

The last four children with thyrotoxicosis treated at the University Hospital were not operated on and all of them achieved complete arrest of symptoms. An examination of Table I shows that the basal metabolic rate of each was within normal range at the time of the last visit to the hospital. Each had also made a very satisfactory weight gain. None of the patients had any signs of toxicity at the time of her last examination. Three of the girls reported recently that, to the best of their knowledge, they were completely well and without symptoms. The fourth complained only of a mild degree of nervousness which did not interfere with ordinary activity. One patient had a residual exophthalmos which was definitely less marked than it previously had been. Three of these children have been observed over a long enough time so that a recurrence of symptoms, while possible, would be unusual and unexpected. The future of the one who was most recently treated is not without the danger of a return of symptoms and will have to be watched carefully for at least another two years.

The medical management of the four patients cited was not the same in each case since there had not been enough information available for the establishment of a routine. All of them received more or less complete bed rest, depending on the severity of the symptoms, during the period of hospitalization. Each also received phenobarbital sedation, the dose being regulated symptomatically. A high caloric and high carbohydrate diet was insisted on in each case. Lugol's solution was given to three children, the amount and duration of administration varying widely in each. The other child received no iodine therapy at any time. Roentgen ray therapy was used in two instances. In both cases it was relegated to the role of an adjunct, given after medical treatment alone appeared to be inadequate, rather than being used with primary intent at the beginning of treatment. The hospitalization periods of the four patients were twelve, thirty-five, ninety-two, and 140 days. These figures, however, do not reflect the true necessity for hospitalization in these patients. It is peculiar to this institution that

TABLE I

DATA CONCERNING THE PATIENTS NOT OPERATED ON

ADMISSION DATE	AGE (YR.)	DURATION OF SYMPTOMS (MO.)	DATA ON ADMISSION TO HOSPITAL	TREATMENT	DATA ON DISCHARGE FROM HOSPITAL	HOSPITAL DAYS	FOLLOW-UP DATA	TOTAL MONTHS OF TREATMENT
Nov., 1940	11	6	Weight, 95 pounds; pulse, 140; B.M.R., +27; chol., 183 mg./100 c.c.	Bed rest, 9 mo.; sedation, 3 mo.; high caloric diet; Lugol's 15 M. b.i.d. for 9 mo.	Weight, 93; pulse, 90	92	Aug., 1941: weight, 110; B.M.R., +1; chol., 178; nervousness; fatigue Nov., 1942: weight, 113; slightly nervous	9
Aug., 1941	13	9	Weight, 105 pounds; pulse, 130; B.M.R., +15; chol., 192 mg./100 c.c.	Bed rest, 2 mo.; sedation, 2 wk.; high caloric diet; Lugol's 15 M. b.i.d. for 10 days	B.M.R., +6	12	Jan., 1942: weight, 125; pulse, 80; no symptoms Nov., 1942: weight, 125; no symptoms	2
July, 1941	15	4	Weight, 94 pounds; pulse, 150; B.M.R., +68	Bed rest, 5 mo.; sedation, 3 mo.; high caloric diet; Lugol's, none; x-ray—July, 1600 r.; Sept., 1200 r.	Weight, 108; pulse, 140; B.M.R., +53; chol., 163	35	May, 1942: weight, 105; pulse, 80; B.M.R., +2; chol., 116; no symptoms Nov., 1942: weight, 106; no symptoms	6
Aug., 1942	13	3	Weight, 100 pounds; pulse, 120; B.M.R., +20; chol., 73 mg./100 c.c.	Bed rest, 10 mo.; sedation, 12 mo.; high caloric diet; Lugol's, 2 M. t.i.d. for 12 mo.; x-ray—Jan., 800 r.	Weight, 123; pulse, 90; B.M.R., +20; chol., 73	140	June, 1943: weight, 119; pulse, 100; B.M.R., +21; chol., 91; nervousness Nov., 1943: weight, 124; B.M.R., +3; chol., 120; no symptoms	12

most of the patient's homes are many miles removed from the hospital. Consequently, it is more convenient at times to retain the patient at the hospital than to transport him back and forth for frequent visits. Also, the patients were kept longer than necessary because we were anxious to observe their courses beyond the period after which it would have been safe to discharge them. The number of months, approximately, during which treatment was continued for each child were two, six, nine, and twelve, the average being seven months. At the end of this time each child was allowed normal activity.

DISCUSSION

It is significant to note that the four medically treated patients cited were the only ones of our series who were given an opportunity to recover without surgery. All the others were "routinely" operated on after the usual ten-day to two-week preoperative period, regardless of their response to medical preparation. There is no way of determining in retrospect how many of the children operated on could have been spared operation, but the indications are that probably many of them could have been treated successfully by conservative management. The length of time required for treatment by medical means was considerably longer than that usually needed for surgical treatment, seven months as compared to six weeks, but we did not feel that this longer period of inactivity was psychologically detrimental to any of the girls. Two deaths occurred in the operated group. It would be only conjecture to say that these might have been averted if surgery had been deferred until the patient was better prepared or if it had been omitted altogether. No report could be found in the literature of any mortalities occurring among medically treated patients or those treated by roentgen ray therapy. Because this series did consist of only a small number of patients, its value cannot be stated in definite conclusions, but it does lend considerable support to those who advocate a trial on medical therapy in place of "routine" operation for children with thyrotoxicosis.

TABLE II

COMPARISON OF PATIENTS OPERATED ON AND THOSE NOT OPERATED ON

	OPERATED ON	NOT OPERATED ON
Number of patients	19	4
Complete relief	9	4
Nearly complete relief	3	
Definite return of symptoms	5	0
Deaths	2	0
Average number of hospital days	35	69
Average number of months of treatment	1½	7

All investigators seem to agree that some children will do well without surgical interference, but they differ in their opinions as to how many will do well. Reilly, whose report is the most recent and most comprehensive, believes that 50 per cent achieve complete arrest of symptoms. Assuming that the percentage is even smaller than that, it would still warrant an adequate medical trial for each patient before surgery should be advised. Every patient must be given a trial because there is no way to foretell which ones will require surgery and which can be treated successfully by conservative measures. Careful study of the patients operated on and those not operated on in our series failed to reveal any single laboratory test or physical sign which could be used as a criterion for prognosticating whether or not con-

servative management would be successful. There was not a close correlation between the metabolic rate or blood cholesterol level and the degree of toxicity as evidenced by the severity of symptoms and response to treatment. The signs and symptoms of toxicity—rapid pulse rate, loss of weight, exophthalmus, tremor, nervousness—are much more reliable than any or all of the laboratory procedures. If these signs and symptoms are mild or only moderately severe, the patient stands a good chance of avoiding surgery if optimal medical care is provided. When medical treatment is being undertaken, close observation of the patient is mandatory. Repeated metabolic determinations and blood cholesterol levels are helpful in following the progress of the patient. The degree of success achieved in any patient treated by medical means will depend to a large extent on the understanding and cooperation of the patient's family. If the child's home is wholesome she can most likely be treated there, with only very short sojourns in the hospital being necessary for the procurement of laboratory data. If conditions are unsatisfactory they will lengthen the period of invalidism and hospitalization and, consequently, may make surgical interference more desirable.

Since we have had practically no experience with the use of roentgen ray therapy in the treatment of childhood hyperthyroidism, little has been said about this form of treatment. In two of our patients not operated on it was used. In one of these, subsequent improvement was definitely related to the therapy. A total of 2,800 r. was administered to this child. The other girl received only 800 r. and no benefit was noted. The roentgenologists are enthusiastic and roentgen therapy is being used more frequently and with greater success in the treatment of adults. Soley and Stone, of the University of California,[4] state that "according to the evidence presented here and elsewhere roentgen therapy can destroy sufficient thyroid tissue in patients with toxic goiter to produce the same results as surgical subtotal thyroidectomy." It is reported that the average length of time required for the arrest of symptoms with this method of treatment is eight and one-half months. Pfahler, of the University of Pennsylvania,[5] estimates that roentgen therapy will result in 65 per cent cures, 25 per cent marked improvements, and 10 per cent failures. More experience in this form of treatment is necessary before statistics regarding its use in children will be available.

SUMMARY

Of twenty-three children with hyperthyroidism treated at the University Hospital since 1925, nineteen were subjected to subtotal thyroidectomies and four were treated without surgery. Included in the group of children operated on were nine complete arrests, three nearly complete arrests, five recurrences, and two deaths. The patients not operated on were all successfully treated by conservative management.

The average period of time for the treatment of the patients operated on was six weeks, while that of those not operated on was seven months. A review of previous reports on the treatment of childhood thyrotoxicosis is presented and the use of roentgen therapy is discussed briefly. It is pointed out that children deserve an adequate trial of medical management before surgery is advised and that in a considerable number of them surgery is neither necessary nor desirable.

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THE ERUPTION OF THE DECIDUOUS TEETH

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THIS study is designed to describe the time when deciduous teeth erupt and to examine some of the factors which may possibly be associated with eruption. Published reports of the time of eruption vary widely and the investigators[3, 9] who have included a measure of variation in their studies have based their conclusions upon small samples.

The data herein described were collected at the well-baby clinics of the Department of Health in the Brownsville and Bushwick Health Districts. They represent all of the white children who attended the seven clinics in these areas from September, 1941, to February, 1942. It is estimated that almost one-third of all children born in these areas are taken to a well-baby clinic for examination within the first year of life. In the Brownsville area, for example, of the 3,600 children born in the district in 1940, 1,060 infants under 1 year of age were registered in the well-baby clinics. The total registration for all ages from birth through 5 years in the four clinics in Brownsville was 3,000 for the year 1940.

The infants were examined by the Department of Health staff physicians, who personally recorded the dental data. Particular care was taken to make sure that each of the physicians understood the meaning of the record chart and was able to distinguish the morphologic characteristics of each type of tooth.*

Since the sample was drawn from the lower income groups it is not representative of the whole child population. It should be noted, however, that there is no agreement as to what effect, if any, socioeconomic status has upon the eruption of teeth. Boas's[4] studies indicate that "unfavorable social conditions bring about the acceleration of eruption of the permanent teeth." On the other hand, Spier,[20] Hellman,[10] and Janoff[11] found that better nutritional opportunities are likely to be manifested by the earlier eruption of the permanent teeth. The study of Sattler[19] seems to indicate that the eruption of the deciduous teeth is likely to be delayed in the children of poorer parents.

It can be said that this sample is representative of the white children who attended the well-baby clinics in these areas of Brooklyn and that despite the low economic status the diets were under regular supervision.

The Description of Tooth Eruption.—Most students of eruption of the permanent teeth have found that the median age (the age at which

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*The definition of an erupted tooth was limited to its appearance through the gums.

50 per cent of the children have the tooth present in the mouth) is a convenient measure of central tendency, and the quartile limits provide a reasonably good description of variation.[5, 6, 7, 14, 15] Several studies[12, 13, 17] have been quite fully descriptive of the eruption of the permanent teeth through the use of a mathematical function. The Medical Research Council group[16] found that the data of eruption were satisfactorily fitted by the equation which describes an autocatalytic reaction. The eruption of the deciduous teeth permits the application of similar techniques.

The best method for the collection of data about growth processes is doubtless a seriatim study of large numbers of children with short intervals of time between examinations. Such a study involves a tremendous amount of labor and would, in the case of eruption of deciduous teeth, extend for at least three years.

The method employed in this study is in the nature of a cross-sectional series. It seems logical to expect that the best estimate of the probability (p) of eruption at any age is represented by the percentage of children in the age group who have that particular tooth visible in the mouth. Conversely, the best estimate of the probability of *not* having the tooth in the mouth (q) is the percentage of children who have not yet shown evidence of tooth eruption. It follows that a series of cross sections at each succeeding month of age is representative of the probability of the eruption of a specific tooth at regular intervals of time. The increase of probability with age may, therefore, be expected to provide a fairly accurate description of the tempo of eruption.*

FINDINGS

It was found that of the 1,962 white children examined no child under 4 months of age had a tooth erupted, while all of the children over 34 months of age had all of their deciduous teeth erupted (Table I).

The estimation of eruption expectation for each month of age for each deciduous tooth was calculated and plotted on probability paper. Approximations of the normal curves were obtained by drawing the best fitting straight line free hand, and the readings transferred to arithmetic graph paper for easier interpretation (Fig. 1).

The order of eruption was found to be fairly constant and conforms with the findings of other studies.[8, 9] Table II lists the expected order of eruption, the median ages, and the quartile limits.

The Number of Teeth Erupted.—The physician or parent is usually more interested in the number of teeth, rather than the specific teeth, to be expected at any age. Fig. 2 and Table III illustrate the rate of increase in the number of deciduous teeth erupted with increase of age. Fig. 2 is a free hand curve through the average number of teeth

*The high correlation in bilaterality of appearance of teeth permits the calculations to be made in pairs.

TABLE I

NUMBER AND POSITION OF DECIDUOUS TEETH ERUPTED AT SPECIFIC MONTHS OF AGE IN WHITE CHILDREN

NUMBER OF CHILDREN EXAMINED AT STATED AGE	AGE IN MONTHS (TO NEAREST BIRTHDAY)	NUMBER OF TEETH ERUPTED AT AGE SPECIFIED BY POSITIONS																			
		UPPER JAW										LOWER JAW									
		RIGHT SIDE					LEFT SIDE					RIGHT SIDE					LEFT SIDE				
		5	4	3	2	1	1	2	3	4	5	5	4	3	2	1	1	2	3	4	5
330	Under 4																				
86	4															1	1				
86	5					3	3									11	12				
95	6				2	3	4	1							1	18	17	1			
77	7				3	12	14	4								30	29				
72	8	1	1	1	5	13	12	6	1	1	1	1	1	1	2	43	44	1	1	1	1
73	9			1	14	32	35	16							6	51	53	6			
74	10		1		25	46	46	25		1			1		13	62	61	14		1	
65	11		3	1	42	51	50	42	1	3			2	2	22	61	60	25	1	2	
56	12		4	2	37	49	51	38	2	3		1	2	1	25	55	55	26	1	3	1
71	13	1	15	1	60	68	69	60	2	18	1	1	18	2	51	69	69	50	2	18	1
119	14		41	7	96	112	115	94	7	45		2	27	3	69	117	116	75	7	32	1
66	15		30	5	59	66	65	59	6	32			25	3	51	66	66	50	2	27	
44	16		32	9	43	44	44	43	10	32			31	9	40	44	44	40	9	32	
43	17		33	14	40	43	43	41	13	34			30	11	36	43	42	37	11	30	
38	18		33	22	38	38	38	37	22	33			32	18	34	38	38	34	19	31	
43	19	1	38	26	43	43	43	43	27	40	2	1	38	26	43	43	43	43	27	39	2
42	20	3	41	32	42	42	42	42	29	41	4	4	40	30	42	42	42	42	31	42	5
42	21	1	40	27	40	42	42	40	27	40		2	40	28	41	42	42	41	28	40	1
35	22	2	35	33	35	35	35	35	34	35	2		35	33	35	35	35	35	33	35	
34	23	4	34	29	34	34	34	34	29	34	5	5	34	25	32	34	34	32	26	34	5
34	24	9	32	31	34	34	34	34	31	32	9	11	32	31	34	34	34	34	31	32	10
42	25	17	42	41	42	42	42	42	41	42	17	18	42	42	42	42	42	42	42	42	16
25	26	12	25	25	25	25	25	25	25	25	13	14	25	25	25	25	25	25	24	25	14
19	27	13	18	18	19	19	19	19	18	18	14	14	18	18	18	19	19	18	18	18	15
21	28	13	21	21	21	21	21	21	21	21	13	13	21	21	21	21	21	21	21	21	13
22	29	18	22	21	22	22	22	22	21	22	18	19	22	21	22	22	22	22	21	22	19
24	30	13	24	24	24	24	24	24	24	24	13	15	24	24	24	24	24	24	24	24	14
24	31	20	24	24	24	24	24	24	24	24	20	22	24	24	24	24	24	24	24	24	22
18	32	17	18	18	18	18	18	18	18	18	17	18	18	18	18	18	18	18	18	18	18
17	33	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17
15	34	14	15	15	15	15	15	15	15	15	14	13	15	15	15	15	15	15	15	15	13
110	Over 34	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110	110
1962	Total children examined																				

erupted at each month of age. In order to visualize the variation to be expected, free hand curves were also drawn through the points representing twice the standard deviations at each age group sample. The resulting band may be expected to include approximately 95 per cent of children.

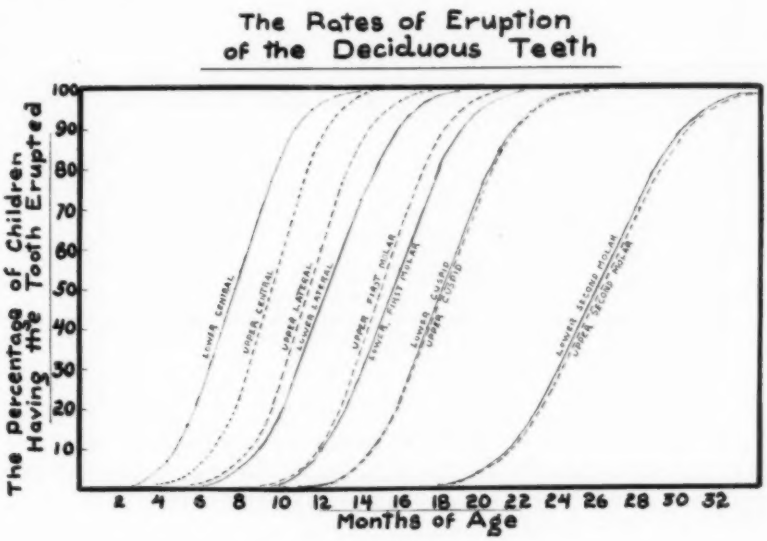

Fig. 1.

Selection by Sex.—Klein and associates[12] and others[5, 14] have found that the *permanent* teeth of females are likely to erupt earlier than those of males. This has not been found to apply to the deciduous teeth. According to Boas[3] the differences in the time of eruption of the deciduous teeth between boys and girls are almost always slight and irregularly distributed so that it would seem that there is no characteristic difference. Doering and Allen[9] came to a similar conclusion.

Table II

The Order of Eruption of the Deciduous Teeth, the Median Ages at Eruption, and the Quartile Limits

Tooth	Months of age		
	First quartile	Median	Third quartile
Lower central incisor	6.1	7.8	9.4
Upper central incisor	8.1	9.6	11.0
Upper lateral incisor	9.9	11.5	13.0
Lower lateral incisor	10.5	12.4	14.3
Upper first molar	13.4	15.1	16.8
Lower first molar	13.8	15.7	17.6
Lower cuspid	16.2	18.2	20.0
Upper cuspid	16.3	18.3	20.2
Lower second molar	23.5	26.0	28.3
Upper second molar	23.7	26.2	28.5

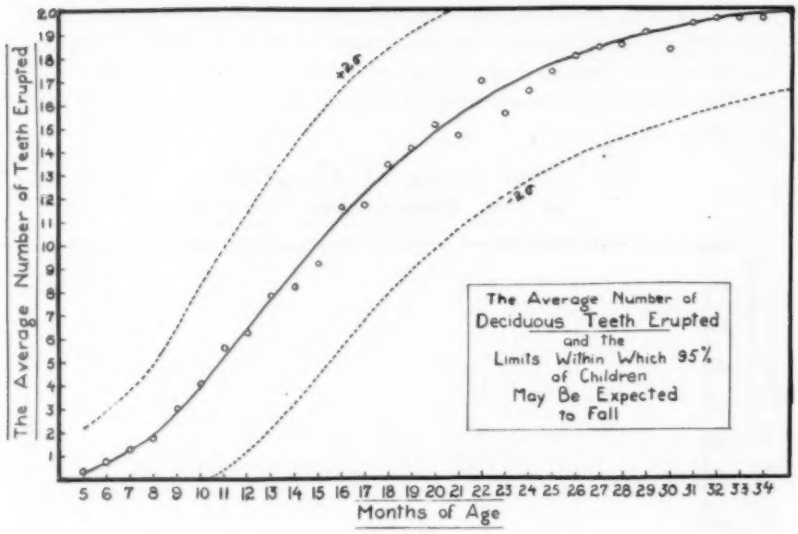
The Average Number of Teeth Erupted
Months of Age
+2.5
-2.5
The Average Number of Deciduous Teeth Erupted and the Limits Within Which 95% of Children May Be Expected to Fall

Fig. 2.

The findings of these data are in agreement with both studies. Table IV shows that while the differences, in general, seem to favor the earlier eruption among boys, the infrequent occurrence of a statistically significant difference does not permit the assumption that the deciduous teeth erupt earlier in either boys or girls. The small differences found permitted the subsequent grouping together of the data of male and female children with reasonable assurance of the retention of homogeneity in regard to the eruption of teeth.

Body Weight and Eruption of Teeth.—Weight as a gross measurement of physical development was available in the data. The relationship between the weight of the child and the number of teeth erupted at any single age was found to be of but slight statistical significance.* It cannot be assumed from these data that the eruption time of the deciduous teeth is associated with variations in physical development as measured by weight alone in a given age period.

The Influence of the Nativity of the Mother on Eruption Time.—A number of investigators[1, 4, 21] have found that there is a significant selection by race and country of origin in regard to the time of eruption of the *permanent teeth.* Such differences suggest that similar differences may be present for the deciduous teeth. It seemed possible that children born of mothers native to the United States may follow a different rate of development than infants of mothers born elsewhere.

*It was found that the correlation coefficient (K) between the number of teeth erupted and the weight of the child for children 14 months of age was +.173 (S.E. = .090); for children 15 and 16 months of age it was +.328 (S.E. = .087); and for children 18 and 19 months of age it was +.270 (S.E. = .104).

TABLE III

THE NUMBER OF WHITE CHILDREN WHO HAD THE SPECIFIED NUMBER OF DECIDUOUS TEETH ERUPTED AT INTERVALS OF ONE MONTH

AGE (MO.)	NUMBER OF TEETH ERUPTED																					TOTAL CHILDREN EXAMINED	AVERAGE NUMBER OF TEETH ERUPTED	STANDARD DEVIATION	STANDARD ERROR OF THE MEAN
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20				
Under 4	330																					330			
4	85		1																			86	.02	.21	.02
5	72	3	9		2																	86	.34	.84	.09
6	66	3	20	2	3		1															95	.70	1.48	.18
7	46	3	14	2	8	1	3															77	1.20	1.73	.20
8	25	5	29	1	6	2	4															72	1.72	1.70	.20
9	15	6	18	4	14	2	7	3	3	1												73	2.96	2.44	.29
10	7	5	14	5	12	9	7	8	6													74	4.03	2.53	.29
11	4	2	7	3	5	4	17	4	16		1		1				1					65	5.55	2.94	.24
12	2		4		9	4	13	6	13	1	2		1					1				56	6.18	2.77	.37
13	3			1	7	3	9	2	22	5	6	3	9								1	71	7.80	2.75	.33
15				1	3	2	6	8	11	4	15	2	15	1	2		4		1			119	8.16	3.36	.32
15				1	3	2	6	8	11	4	8	1	17	1	2		2					66	9.22	2.92	.36
16							2	1	6	2	4	2	12	2	6	1	6					44	11.63	2.84	.43
17					1		2	2	5	1	5	1	11	1	4		10					43	11.65	3.30	.50
18							1	1	3		3		8		4		17	1				38	13.45	3.09	.50
19							1				1		14	1	3	2	19	1	1			43	14.11	2.42	.33
20									1			1	7	2	3		23		1	2	2	42	15.13	2.46	.38
21					1				1				9		5		24	1		1		42	14.55	2.62	.40
22													1	1			22		2		9	35	16.92	2.07	.39
23											2		4		2		20	1	1		4	34	15.60	2.47	.42
24									2				1				19	3			9	34	16.55	2.87	.46
25													1		1		21	2	1		16	42	17.40	2.12	.33
26															1		10		1	1	12	25	18.05	2.09	.42
27							1										3		2		13	19	18.40	3.00	.69
28																	8				13	21	18.45	2.11	.46
29													1				2		1		18	22	19.16	1.97	.42
30																	9	1	1		13	24	18.27	1.90	.39
31																	2		2		20	24	19.46	1.21	.25
32																	1		1		16	18	19.65	1.03	.24
33																			3		14	17	19.62	.83	.21
34																			3		12	15	19.60	1.20	.32
Over 34																					110	110	20.00		
Totals	657	27	118	24	79	29	91	51	109	20	47	11	112	9	33	3	223	10	21	5	282	1962			

TABLE IV

THE DIFFERENCES IN THE AVERAGE NUMBER OF DECIDUOUS TEETH ERUPTED IN MALE AND FEMALE CHILDREN AT INTERVALS OF 1 MONTH OF AGE

AGE (MO.)	AVERAGE NUMBER OF TEETH ERUPTED		DIFFERENCE / σ DIFFERENCE
	MALE	FEMALE	
4	0	.05	.7
5	.44	.22	1.2
6	.83	.62	.8
7	1.40	.83	1.5
8	1.82	2.00	.3
9	3.22	2.78	.8
10	3.93	4.16	.4
11	5.59	5.49	.1
12	6.56	5.82	.8
13	8.13	7.60	.7
14	8.63	7.88	1.2
15	10.23	8.22	3.3
16	11.70	11.77	.1
17	11.36	12.00	.7
18	12.75	13.23	.5
19	14.35	14.04	.4
20	15.30	14.77	.7
21	14.90	14.10	1.0
22	16.56	17.20	.9
23	15.38	16.00	.6
24	16.40	16.77	.4
25	17.70	17.28	.6
26	19.28	17.50	2.3
27	20.00	17.10	2.3
28	19.00	18.14	1.0
29	19.60	18.80	.8
30	18.10	18.50	.5
31	19.45	19.65	.4
32	19.25	20.00	1.4
33	20.00	20.00	.0
34	19.70	19.00	.7
35	20.00	20.00	.0

The limited data available in this study precluded analysis by specific country of origin of the parents as the numbers were reduced to unreliable limits. However, as between children whose mothers were native-born and those foreign-born, no significant differences could be observed in the time of eruption of the deciduous teeth.

SUMMARY

The examination of 1,962 white children of fairly low economic status but under regular nutritional and medical supervision in a well-baby clinic, during the fall and winter of 1941-1942, provided material for a study of the eruption of deciduous teeth. The proportion of children who may be expected to have each type of tooth erupted was calculated for each month of age and smoothed curves plotted. The number of teeth to be expected at any age was also calculated and plotted together with a measure of variation to be expected.

It was found that no deciduous teeth had erupted in children under 4 months of age and that all of the deciduous teeth had erupted in all

of the children over 34 months of age. The most usual order of tooth eruption was found to be from earliest to latest; lower central incisor, upper central incisor, upper lateral incisor, lower lateral incisor, first molars (either upper or lower), cuspids (either upper or lower), and second molars (either upper or lower).

There seemed to be no characteristic difference between boys and girls as to the ages at which specific teeth erupt, nor in respect to the number of teeth to be expected at any age.

The relationship between variations in the weight of the child within an age group and the rapidity with which teeth erupt was small and of no statistical significance.

No significant difference in eruption time was observed whether the child was born of a native-born mother or of a foreign-born mother.

So many of the Department of Health staff were of assistance in the collection of the data, that limitation of space prevents their enumeration. It is with grateful appreciation that I specifically make mention of the encouragement, advice, and patient criticism of Dr. Leona Baumgartner, Director of the Bureau of Child Hygiene, Dr. Myron E. Wegman, and Mr. Harry Goode, and the cooperation of Miss Amelia Grant, Director of Nursing, and Dr. Harry Strusser, Chief of the Dental Division.

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TREATMENT OF VASCULAR NEVI

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BECAUSE of the confusion as to the proper treatment of vascular nevi, I believe that a review of the various methods is justified. Each year numerous articles are published which deal with the treatment of these lesions. Most of the authors recommend early treatment and the use of x-rays or radium when dealing with vascular nevi of infancy.

I do not believe that vascular nevi should be treated before the age of 6 years because the vast majority of these will have involuted spontaneously by that time. I do not believe that x-rays or radium should be used in their treatment.

Vascular nevi may be classified into two groups:

A. Vascular nevi involuting spontaneously by the age of 6 years without treatment. These are present at birth or appear shortly thereafter. They usually grow quite rapidly, attain their maximum growth in a few weeks to a few months, always cease growing by the age of 1 year, vary in size from that of a dime to that of a lesion covering one side of the head or an extremity, and undergo involution spontaneously by the age of 6 years. This group may be subdivided as follows:

1. Strawberry angioma—The lesion is scarlet to deep purple in color, has an irregular tufted surface, is somewhat elevated and is situated in the cutis.

2. Cavernous angioma—This lesion lies in the subcutaneous tissues, is soft, round or lobulated, varies from a faint to a deep blue shade, and may be level with or arise above the surface of the skin.

3. Combined strawberry and cavernous angioma.

This group of vascular lesions is usually treated by the application of solid carbon dioxide, by radiation with x-rays or radium, by the injection of sclerosing agents, by surgical excision, or by electrodesiccation. Any of these methods will yield satisfactory results in as much as these lesions always disappear without treatment if left alone. Any of the above-mentioned methods of treatment, however, may scar the skin. X-rays and radium may produce atrophy and telangiectasia of the skin and disturbance of bone growth. The use of radium and x-rays about the eye may produce cataract. When the natural history of these nevi is taken into consideration, one is not justified in introducing the hazards and expense of treatment of these benign lesions. The physician who sees these lesions and the parents of the patient may be frightened by the rapid growth and extensiveness of some of the lesions, especially if a side of the face, the nose, the eyelid, or an extremity is involved. The physician and the apprehensive parents may be stampeded into seeking and demanding treatment. However, the best interest of the infant is

served by withholding treatment. The physician should be reassured by the knowledge that these types of vascular nevi are not seen in the adult, not because all of these lesions are treated in infancy, but simply because they disappear spontaneously.

In 1938, Lister* discussed this group of vascular nevi in a very comprehensive article which should be read by every physician who has occasion to see or treat these lesions. He followed ninety-three strawberry angiomas for a period of from one to seven years and found that these nevi always disappeared by the fifth year of life. Since his article appeared, I have found my experience to be the same, and I have given up entirely the treatment of these lesions.

B. Vascular nevi not involuting by the age of 6 years.

1. "Spider nevus"—This consists of a central dilated vessel with radiating tributaries. It appears at any age. It is treated best at the age of from 10 to 12 years by electrolysis or electrodesiccation.

2. "Port wine mark" (nevus flammeus)—This is a red to purple area of erythema, commonly situated on the side of the face or neck. The area may be elevated and occasionally nodular. The color is not obliterated on pressure. It is present at birth. Occasionally it is associated with intracranial vascular lesions or contralateral vascular lesions of the trunk and extremities. There is no satisfactory treatment, although plastic surgery is occasionally successfully employed. Occasionally, at puberty or pregnancy, these lesions will grow and become nodular. They do not respond to x-ray or radium therapy.

3. Nevus flammeus nuchae—This consists of a pink to red macular area in the nuchal region, which may persist indefinitely, or may fade as the child grows older. No treatment is beneficial or necessary.

4. Single or multiple blue to red vascular lesions, sometimes called cavernous nevi, usually present at birth—There is no rapid growth and growth is in conformity with the growth of the individual. These may remain stationary in size or may grow at puberty or during pregnancy. These may be associated with visceral and muscular vascular lesions. These do not respond to x-ray or radium therapy. They are best treated by injection of sclerosing solutions or by electrocoagulation.

5. Congenital varices of the arms, legs, etc.—These are treated with injections of sclerosing solutions or by ligation. They do not respond to x-ray or radiation therapy.

CONCLUSIONS

Vascular nevi of infancy should not be treated before the age of 6 years. Spontaneous involution will have occurred in the majority of the lesions by that age. X-rays and radium have no place in the treatment of vascular nevi of infancy.

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*Lister, W. A.: Lancet 234: 1429, 1938.

COR BILOCULARE

Report of a Case

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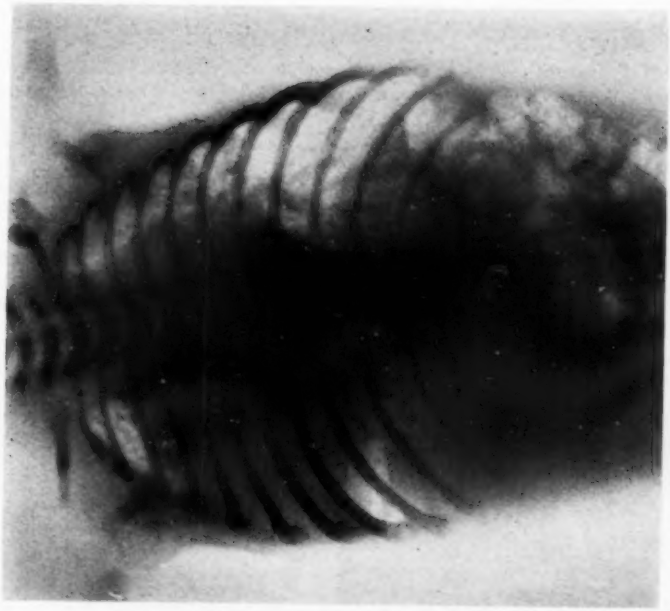
THERE is a paucity in the literature of cases of cor biloculare, a rare congenital cardiac anomaly. In 1936, Abbott,[1] in analyzing 1,000 cases of congenital cardiac anomalies, found only nine true cases of cor biloculare and five additional cases associated with other defects. By 1942, only thirty-seven cases had been reported.[2] Similar hearts have been described by others.[2-11] Giustra and Tosti[10] reported a case of true cor biloculare in identical twins. According to most authors there is evidence in cases of cor biloculare of septal vestiges, either in the atrium or ventricle; thus, the term cor biloculare, or "amphibian heart," refers to function rather than to anatomical structure. Most of the cases reported also showed other congenital anomalies. Due to arrest in development the heart is frequently displaced to the right side of the body. Although cor biloculare is one of the morbus coeruleus, we were unable to find any constant association of cyanosis with the disease. The oldest patient reported is a girl who died at 16 years of pulmonary tuberculosis.[11] The functional mechanism of cor biloculare is described by Wood and Williams.[7]

CASE REPORT

A full-term, white, female infant, weighing 6 pounds 6¼ ounces, was born Nov. 22, 1942. The past familial history and physical examination of the mother, a primipara, aged 27, was insignificant. The birth was precipitate. Cyanosis of the entire body was present at birth. On Nov. 25, 1942, three days after birth, x-ray (Fig. 1) revealed a normal thymic shadow. The heart lay in the right chest. The liver was also on the right. There was present a fracture of the left clavicle with slight displacement of its outer third. The cyanosis gradually cleared and the infant was sent home Dec. 2, 1942. While at home the baby was subject to severe crying spells, but the mother did not observe whether this affected the cyanosis. The baby nursed poorly and was dyspneic during feeding. The infant was well until 5:00 P.M. Dec. 5, 1942, thirteen days after birth, when cyanosis and dyspnea became marked and her cry became very feeble. On admission to the hospital, on the same day, the infant was cyanotic and grunted with respiration. The respirations were 84 per minute. There was marked dullness over the entire right chest anteriorily and posteriorly. The heart tones were louder over the right chest. No murmurs were heard. There were fine crepitant râles over the upper and lowermost portions of the right chest posteriorly and anteriorly and at the apex. The breath sounds were high-pitched but less intense over the right suprascapular area posteriorly than over the left. There was a bluish discoloration to the sclera. Complete blood count revealed: hemoglobin, 13.9 Gm.; 96 per cent (Sahli); red blood count, 4,300,000; white blood count, 10,200; segmented, 34 per cent; nonsegmented, 2 per cent; lymphocytes, 62 per cent; monocytes, 1 per cent; eosinophiles, 1 per cent. X-ray picture (Fig. 2)

From the Pediatric Service of Dr. E. Rush and the Pathological Laboratories of the Mount Sinai Hospital.



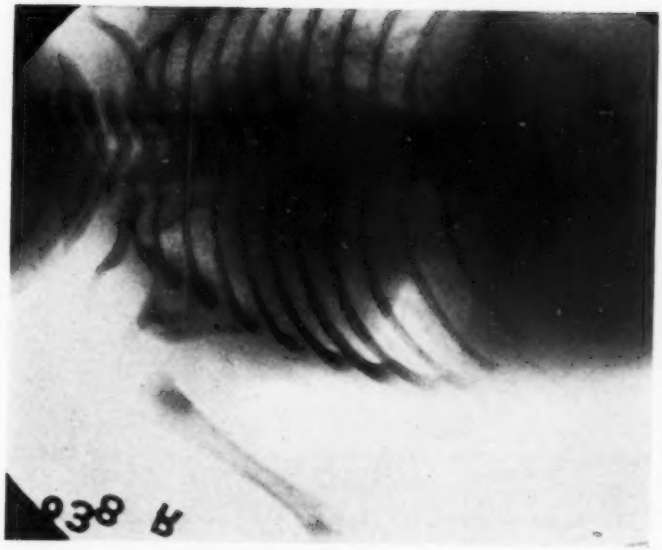


Fig. 1.—X-ray taken three days after birth showing congenital heart in right chest. Note presence of liver on right side.
Fig. 2.—X-ray taken on day of death showing essentially same findings as in Fig. 1.

taken Dec. 15, 1942, revealed little change from that taken Nov. 25, 1942. The infant died Dec. 15, 1942, of cardiac failure.

AUTOPSY

External Examination.—The body was that of a white, female infant, with the given age of 23 days, measuring 42 cm. and weighing 3,020 Gm. The lips and fingernails were cyanotic.

Internal Examination.—The subcutaneous fat was normal in amount. There were 100 c.c. of light yellow fluid in each pleural cavity. The pericardial sac contained 50 c.c. of light yellow fluid. The abdominal cavity contained no excess fluid. The domes of both diaphragms reached to the fourth interspace. The thymus was normal in size. The heart lay in the right chest cavity anterior to the right lung and was enlarged. The right lung was much smaller than the left. This was due principally to almost complete compression of the right lower lobe and to partial compression of the other lobes. Its parenchyma was congested throughout. The lower lobe of the left lung was partially atelectatic and partially consolidated. The remainder of the lung was congested. Except for the heart, the other viscera were essentially normal.

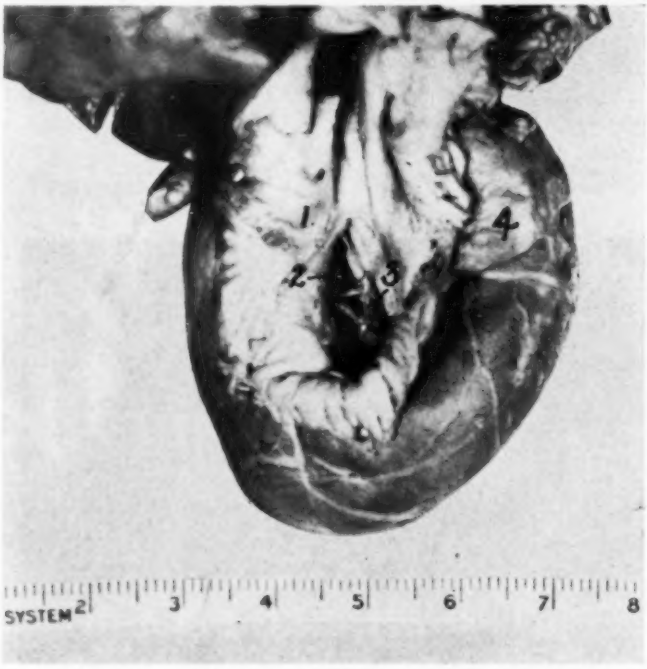


Fig. 3.—Showing single auricle, *1;* communicating auriculo-ventricular septum, *2;* tricuspid valve, *3;* and auricular appendage, *4*.

Heart.—The heart, as stated, lay chiefly in the right side of the chest, compressing the right lung laterally and posteriorly. The heart was large. It measured 5 by 4.5 by 3.5 cm. It consisted entirely of two roomy chambers (Fig. 3), one auricle and one ventricle, the ventricle lying anteriorly and the auricle posteriorly. The ventricular chamber was much larger than the single auricle. Emerging from the upper portion of the single ventricle was a large vessel which

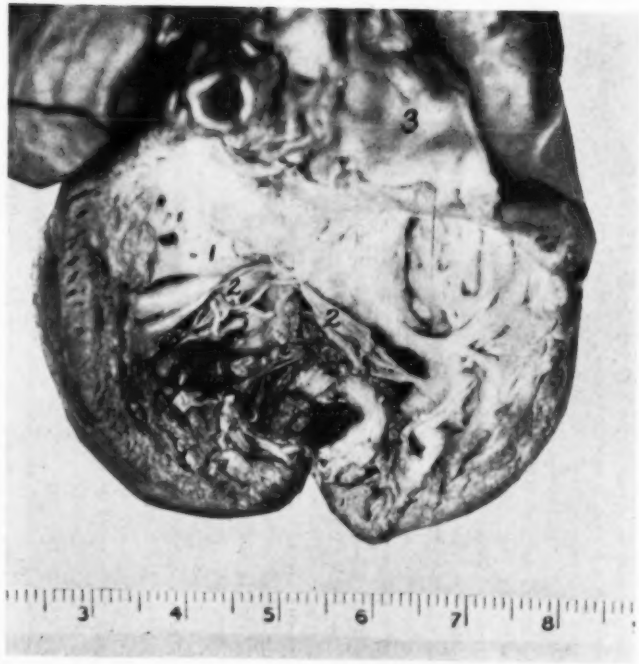


Fig. 4.—Showing hypoplastic systemic aorta, *1*.
Fig. 5.—Showing dilated single ventricular chamber, *1*; auriculoventricular cusps, *2*; and pulmonary aorta, *3*.

divided into branches to the right and left lungs, 1.5 cm. from its origin. The vessel measured 2.5 cm. in circumference. Almost immediately beyond this site it continued, considerably reduced in size, measuring at this point only 1 cm. in circumference. In this narrowed state it represented a large ductus arteriosus. Two centimeters beyond its origin, this ductus arteriosus joined the small systemic aorta. At the orifice of the large emergent artery, just described, were three normal semilunar valves. No coronary vessels emerged from these, identifying the artery as the pulmonary aorta.

To the right of the pulmonary aorta a small systemic aorta emerged (Fig. 4). It communicated through a greatly constricted orifice 0.5 cm. in diameter with the single ventricle passing under a ledge of muscle wall and emerging into the left ventricle 1 cm. below the pulmonary orifice. It was guarded by three cusps, from two of which emerged two small coronary vessels. These cusps were reduced in size, being about one-half the size of the pulmonic cusps. Though this systemic aorta communicated with the single ventricle through a definite orifice, the nature of its communication with the ventricular chamber makes it highly probable that the aorta, in its first portion at least, was functionally atretic. The systemic aorta averaged 1.2 cm. in circumference. It ascended and arched laterally where it was joined by the dilated ductus arteriosus as previously stated. From its arch, there emerged the normal arterial branches to the body.

The wall of the auricle was thin, measuring 1 mm. in diameter, that of the ventricle 5 mm. The ventricle appeared moderately dilated (Fig. 5). The endocardium of the ventricle was yellowish and appeared thickened. The muscle appeared normal. Between the auricle and the ventricle was a tricuspid valve (Fig. 3). Two of the cusps were normal in size; the third was rudimentary. The single auricle was roomy and possessed two appendages, a right anterior and a left posterior. Into its posterior portion entered two large veins from the lungs and the superior and inferior vena cavae. From the anterior wall there arose a ridge which projected partially into the cavity. Below this was the orifice of the coronary sinus with its primitive valve.

SUMMARY

The clinical course and autopsy findings of a 23-day-old female infant are described. There were no other somatic anomalies other than those relating to the cardiovascular system. These were:

1. Displacement of heart into right chest cavity.
2. Cor biloculare with dilatation.
3. Hypoplastic systemic aorta with virtual functional atresia.
4. Persistent prominent ductus arteriosus.
5. Ventricular endocardial fibrosis.

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LYMPHOBLASTOMA IN CHILDREN UNDER THIRTEEN YEARS OF AGE

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BECAUSE of the general impression that cancer is a disease associated only with old age, the frequency with which cancer occurs in childhood is quite often overlooked. Indeed, the United States census of 1939 reported that 1,103 children under the age of fifteen died of cancer, or about 0.7 per cent of all deaths from cancer in this country.

Pearl and Bacon,[1] in 1927, reported on a review of 6,670 autopsies at Johns Hopkins University in which they found 816, or 6 per cent, malignancies in patients under 20 years of age.

Hoffman[2] noted that as a rule tumors in youth are of the sarcoma type and that neoplasms of early life are more rapidly fatal than in later years. Reporting,[3] in 1937, on cases of soft tissue sarcomas treated by us at Bellevue Hospital, we noted that four of the seventy-eight sarcomas were in patients under 16 years of age.

In 1939, Pack and Anglem,[4] in a review of their cases at Memorial Hospital, found 100 patients under 16 years of age with tumors of the soft tissues, ten of whom had unclassified types of tumors.

Kellert,[5] in 1939, reviewing the cancer cases reported in Schenectady, N. Y., found fifteen cases in children 15 years of age and under. He also cited DePort's[6] statistics for 1937, showing that of 8,904 reported cancer cases in New York State outside of New York City, twenty-six were in patients under 15 years of age.

Quite logically it might be suggested that tumors of the young should prove more active than those in adults. There is, however, the question whether malignant neoplasms in children represent a congenital neoplastic development within the child's tissues as a continuation of embryonal growth. In a review of 300 necropsies Wells[7] found no evidence of congenital neuroblastomas. He ventures to doubt the authenticity of the reported cases of congenital leucemia, for, as he says, no definite proof has as yet been offered of transfer of lucemia from mother to infant. In 1932 Kaplan and Connery[8] reported on a pregnant patient with leucemia treated by irradiation who gave birth to a normal child free of leucemia.

Although the Radiation Therapy Service at Bellevue Hospital draws upon one of the largest groups of patients in the free general hospital category, only a very small number of young patients with neoplastic diseases have been referred for treatment during the past twenty years. This may be explained as being due to the economic status of the type of

From the Department of Radiation Therapy, Bellevue Hospital.

patients coming to a municipal general hospital, to the late stage of the disease in which the children are usually received, and to the fact that usually children with leucemia, when brought to the clinic, already manifest an acute condition.

Because neoplasms of children are usually of the highly cellular type we should note a preponderance of lymphoblastomic types of malignancies. In our grouping we have considered the age of 13 years as the limit of our study in this report, children over this age being more liable to neoplastic disease.

Of the twenty-seven patients with lymphoblastomas in children 13 years and under referred to the Radiation Service for treatment, there were ten patients with leucemia, eleven with Hodgkin's disease, and six with lymphosarcoma.

Of those with leucemia there were seven patients with the lymphatic and three with the myelogenous type. There were six boys and four girls, the youngest 13 months and the oldest 6 years of age. There was one 1 year of age, one 2 years, one 2½ years, three 3 years, one 5 years, one 6 years of age, one 13 months, and one not stated.

Although many Negro children are admitted to Bellevue Hospital for various ailments, there were none in our group of patients with leucemia. In most instances the children complained of pain in the joints and manifested general weakness; some had "purpuric spots" over the body. Some had generalized adenopathy. All showed a marked pallor. The spleen was palpably enlarged in all but one patient. The blood count was indicative of the condition in all patients, and the highest white cell count was 88,000. Fever was present in most instances. All patients were treated with x-ray therapy. There was temporary relief in all patients. The longest known period of survival was four months after treatment. Two died—one, one month after treatment, and one, three months after treatment. Final results in the other cases were not recorded.

In the eleven patients with Hodgkin's disease it was noted that the age at diagnosis was older than in those patients with leucemia. The oldest was 13 years and the youngest was 1½ years old. Boys predominated; there were nine boys and only two females in this group. There were four 8 years and four 10 years old. Their years were, one each, 1½, 3, and 13 years old, respectively. There was one Puerto Rican and one Negro child in this group.

The most common symptom complained of was swollen nodes, especially of the neck, which were present in six patients. In one patient the complaint was a large swelling in the groin. In one the symptoms were pain in the leg, fever, and weakness. In one fever and gradually enlarging abdomen with respiratory distress were the complaints. The palpable nodes were usually discrete, massive, and freely movable. The spleen was palpable in four patients and the liver in one. X-ray examination showed the chest involvement in three patients, mostly

manifested by mediastinal infiltration. In one patient the x-ray findings were extensive. This patient, a girl 10 years of age, had had fever for six months and enlarging abdomen for three months. The x-ray of the chest showed a dense shadow in the right lung and in the upper lobe extending from the hilus to the apex and obliquely out to the axilla. In the middle of this shadow another denser shadow was noted adjutant to the spine, suggesting displacement of the mediastinum.

Diagnosis in all patients was confirmed by biopsy. Treatment was by high voltage x-rays, either to the involved node areas and/or to the chest. In some patients treatment was given to the spleen. Of the eleven patients followed, seven are known to be dead.

There were only six patients with lymphosarcoma under 13 years of age referred to us for treatment. All were white children, four boys and two girls. The youngest was 6 months, the oldest 6 years. Three had chest symptoms and three, neck swellings. Three complained of associated abdomen swellings; one had a chest involvement and one, a neck node. One patient with neck nodes had severe, frontal headaches and back pains. In three patients the spleen was palpable; in two, the liver. In one the right eye and lids were involved. Biopsy proved the diagnosis in five patients.

In one patient rapid death occurred during treatment and an autopsy was permitted. This case is of interest because even following autopsy it still remains not entirely settled whether it was leucemia or lymphosarcoma transformed into leucemia. The details of this case were as follows:

J. B., a white boy 5 years of age, entered the hospital March 7, 1927, complaining of respiratory distress. He had been transferred from another hospital where he was treated for bronchitis and pleurisy and where a diagnosis of possible leucemia was made. Examination on admission showed a pale youngster with abdominal distention and an enlarged, hard spleen and generalized adenopathy. He had marked difficulty in breathing, and an x-ray of the chest showed a very extensive dense mediastinal mass. The blood count was not accurate because of dehydration, but it showed a 70 per cent lymphocytosis and only 20 per cent polymorphonuclear cells. A provisional diagnosis of lymphosarcoma was made. On March 18, 1927, x-ray treatment was administered to the mediastinum to relieve respiratory distress. He responded poorly and further irradiation was withheld. On April 19, 1927, because of increasing distress, irradiation was again instituted. Just as the x-ray was to be administered the boy expired. Autopsy April 20, 1927, showed a large tumor of the mediastinum, generalized adenopathy, and enlarged liver and spleen.

Autopsy Report.—The autopsy report, in part, was as follows:

Thorax: On opening the thorax, a large amount of yellowish, clear fluid escaped from both pleural cavities. The anterior mediastinum was filled by a large, lobulated, whitish tumor, intimately adherent to, but not infiltrating, the sternum. It extended from the suprasternal notch above the diaphragm below and along the ribs of the lower thorax for 2 or 3 cm. and measured 16 cm. in length, 10 cm. in width, and 8 cm. in depth at its thickest point. On section, this mass was of a homogeneous yellowish white color, studded with occasional partly circumscribed

nodules of a more distinctly yellowish tint. The innominate veins and greater vessels were surrounded by this growth which crossed the hilum of the lungs and extends posteriorly to the heart for a short distance. The mass was intimately adherent to the parietal pericardium but apparently had not perforated it at any point. The pericardium is surrounded by it, except for one or two oval spots. The tumor tissue divided at the pericardial attachment to the diaphragm and spread in an even layer over the median portions of the diaphragmatic pleura and along the vertebral column. In no place does the bone appear to be involved.

Microscopic Diagnosis:

Tumor of mediastinum: This tumor was composed of masses of closely packed, small round cells, all fairly uniform in size, having rounded, dense nuclei and little cytoplasm. Occasionally the cells assumed a parallel row arrangement, but in most of the areas the growth was diffuse. Mitoses were rare. The tumor was fairly well vascularized but the necroses were frequent; no giant cells were seen. The lesion resembled leucemic infiltration rather more than so-called lymphosarcoma, although this was a debatable point.

Spleen: The splenic architecture was preserved, but the follicles were very indistinct due to the fact that the pulp was filled with small, round cells with which they seemed to merge. The round cells of the pulp resembled lymphocytes and were the predominant cell present, although monoblasts and monocytes were also encountered; no necrosis was seen.

Lymph Nodes: Cervical, thoracic, abdominal, and inguinal nodes were all similar in appearance. There was diffuse infiltration of lymphocytes with practically complete loss of node architecture. The process did not appear to have broken through capsules, but fatty areolar tissue about them was diffusely infiltrated by lymphocytes.

The pathologist's opinion based on his findings was as follows: This case probably was one of lymphatic leucemia, with formation of leucemic tumor in the mediastinum, rather than leucemia secondary to a tumor. This point was of course open to question.

In this group of six patients, three are known to be dead, and in three instances the final outcome could not be noted because the family could not be located after leaving the hospital and these patients are presumed to be dead.

Since, as Bergonie and Tribondeau[9] have axiomatically established, the more embryonal the tissue, the more responsive it is to irradiation, it would naturally be expected that neoplasms in childhood should be quite radioresponsive and that, as Sittenfeld[10] has stated, "Irradiation has a definite field of usefulness, especially in the treatment of lymphoblastomas."

Nevertheless, the results achieved have not been very favorable, especially in leucemias. In most instances leucemia in children is an acute condition, usually with rapid mortality. As a rule, clinicians are averse to giving radiation a trial in acute leucemia, although it is not unreasonable to hope that such therapy may have a favorable result in this condition which is virtually fatal. As no other treatment is effective and no harm is done by irradiation, it would seem logical that this form of therapy be tried. Moreover, there is now no question that in the treatment of chronic leucemia irradiation is the method of choice,

and while it does not effect a cure, it may at least prolong the life of the patient for many years.

Stout[11] emphasizes what clinical radiotherapists have long noted, that in lymphosarcoma one may expect longer survival in older patients than in those under 20 years of age. The more localized the involvement, the more permanent the control, and, as in all types of malignancy, the earlier the recognition and the more adequate the treatment, the more hopeful the prognosis. Giant follicular type lymphosarcomas, Symmers[12] and Rubenfeld[13] have shown, are least malignant. Irradiation is the best treatment; if surgery is used, roentgen therapy should follow.

Not long ago the development of radioactive substances led to the belief that a new, more effective method of treatment for lymphoblastomas was at hand. Kenney,[14] however, considers treatment of lymphosarcoma with radioactive substances experimental. While in a few instances it seems to be effective, it is not free from grave uncertainties and hazards and the results are, as yet, too indefinite to warrant its replacing proved irradiation methods.

The same criticism applies to the use of such methods for the treatment of leucemias and Hodgkin's, disease whereas Tuttle, Erf, and Lawrence[15] state that radioactive substance therapy has not proved effective. For this condition, irradiation should be used, in accordance with proved methods. The best radiation technique is still undetermined, for advocates of both small and heavy doses show equally good results. The customary pessimism in connection with Hodgkin's disease is not warranted according to Slaughter and Craver,[16] who present a more hopeful outlook, especially when the lesion is limited. Their suggestion, not altogether original, the surgical removal of isolated masses, offers a chance for increasing beneficial results.

Desjardins[17] points to failure of irradiation in Hodgkin's disease and lymphosarcoma as due to insufficient attention to anatomic arrangement of treatment with reference to site of symptoms, distribution of the treatment, quality of rays, and pathologic and clinical factors related to the stage of the condition. Careful attention to these factors cannot but ameliorate, and sometimes will soon arrest, the condition.

In children under 13 years of age, however, our experience has not proved very hopeful. Perhaps because of the age, the lymphoblastomas are made more virulent and active. The usual inherent resistance or perhaps acquired resistance to these neoplasias is absent in such young children. The tissue-growth stimulus, whatever it may be, is evidently enhanced in youth, and this stimulus is transmitted to neoplastic, as well as normal, cells, permitting their overpowering effect before the child can acquire the immunity or inhibitory quality found in older persons affected by malignant lesions.

Possibly, too, we have not achieved technically the best method of treating these patients. Greater attention to supportive therapy and a more gradual over-all irradiation may perhaps prove more successful. The toxemia following irradiation in small children is a serious sequel not to be casually overlooked.

However, since no other method of treatment offers any more optimistic outlook, irradiation is as yet the only therapeutic agency susceptible of development with more successful possibilities.

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OSTEOGENESIS IMPERFECTA AND OSTEOPSATHYROSIS

A Contribution to the Study of Their Identity and Their Pathogenesis

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CONGENITAL fragilitas ossium is a disease of the connective and supporting tissues comprising a number of features: multiple fractures occurring mostly during childhood and caused by relatively slight injury; narrow shafts of long bones; excessive formation of callus; blue sclerae; blue tympanic membranes; formation of "fishtail vertebrae"; abnormal values of calcium and inorganic phosphorus in the serum; progressive deafness in middle life. Other symptoms which occur more rarely in association with this disease will not be discussed in the present communication. Fragilitas ossium tends to have a familial occurrence, suggesting a genetic component in its pathogenesis. Some of the patients are born with fractures, others sustain them only later in life. There are cases which show merely the typical alterations of the osseous system and of the sclerae without associated fractures at any time during the patient's life. In still others the only sign of the disease is the blue discoloration of the sclerae.

The question whether the "early type" with intrauterine fractures (osteogenesis imperfecta, type Vrolik) is essentially different from the "late type" with only postnatal fractures (osteopsathyrosis, type Lobstein) is as yet unsolved. Pathogenesis is likewise indeterminate. Both of these problems will be discussed, as well as that of therapeutic indications.

Of the authors who sponsor the duality of the two syndromes, the most outspoken is Glanzmann.[1] In his opinion the "early type" is not hereditary; the limbs are shortened (micromelia), the cranium consists only of small islands of bony structure, the calcium level in the serum is elevated, the concentration of serum inorganic phosphorus is at the upper limits of normal, and the total duration of life rarely, if ever, exceeds four years. He regards the "late type" as a qualitatively different disease in that the body proportions are normal; the bony deformities are found in the middle of the shafts, the cranium is unyielding, the calcium level in the serum is normal, serum inorganic phosphorus is low, and life expectancy is not curtailed. Similarly, Funk[2] stated explicitly that cases of osteopsathyrosis (Lobstein) never occur together with cases of osteogenesis imperfecta (Vrolik) in the same family. According to his experience, in juvenile osteopsathyrosis the serum alkaline phosphatase values lie above the normal range.

The following case histories may contribute to the elucidation of the relationship between the two disease syndromes:

CASE 1.—E. S., the first child, was born Feb. 2, 1925. The father was 35 years of age, the mother 25. On the maternal side several instances of fracture have occurred. The mother suffered a "spontaneous" fracture of the left femur at the age of 2½ years; she was of short stature and suffered from deafness. A maternal aunt had sustained four femoral fractures prior to the age of 17 years; the great-grandmother experienced five femoral fractures during the later years of her life. The patient, born by normal delivery, was found to have a fracture of the right femur which was considered to have been most probably of intrauterine origin. There was also a greenstick fracture of the sixth rib near the sternum; both parietal bones were abnormally soft, and the right one had a fracture line. Otherwise the patient's neonatal condition was satisfactory.

She was breast fed and was kept under observation for six months, during which time in spite of an otherwise uneventful course she suffered the following additional fractures: At 33 days, right humerus at its distal extremity; at 55 days, right humerus at its proximal end; at 84 days, right femur at its proximal end; at 6 months, left femur at its distal end.

Roentgen examination showed the cortex of all the long bones to be delicate and the osseous structures in general somewhat deficient in calcium. Healing of the fractures was invariably accompanied by excessive callus formation. Signs of rickets were absent, and during the entire period of observation the abnormal structure of the bones remained unchanged.

CASE 2.—H. S., the second child of the same family, was born April 9, 1926, by normal delivery. Although his general condition was satisfactory, the anterior fontanel was abnormally wide, and the cranial sutures were separated. The parietal bones were pliable and showed small defects at the tubera. There was a recent fracture of the left femur, which in the course of time became surrounded by abundant and dense callus, and a fracture of the right femur which was thought to be of earlier origin. One of the tenth ribs contained a fracture close to the sternum. Roentgen examination disclosed ground-glass atrophy of the entire skeleton; there were no rachitic changes. The patient's further development was uneventful, and no additional fractures were found. The defects in the parietal bones remained open for three months.

These children thus come from a typical Lobstein family in which three previous cases of fragilitas ossium are known to have occurred, including that of their own mother. All of the fractures incurred by the ascendants were of postnatal origin, and the three women concerned survived the first decades of life. In the case of the two infants described there is the highest likelihood that they suffered from intrauterine fractures and likewise exhibited the other characteristics of osteogenesis imperfecta (Vrolik). Both children survived their fifth year. In short, they represent noteworthy divergences from the concept of Glanzmann[1] who regards the Vrolik type and the Lobstein type as two fundamentally different diseases. Additional examples of Vrolik cases in Lobstein families are cited by Riesenman and Yater.[3]

CASE 3.—S. G., born March 19, 1930, was admitted Oct. 17, 1937, at the age of 7½ years. An older brother was in good health; a younger brother is described as Case 4. No instances of multiple fractures or of deafness were known in the ascendants. The patient had suffered a "spontaneous" fracture of the right leg at

the age of 1 year, from which she had made an uneventful recovery. Subsequent fractures occurred as follows: right leg at 2½ years, right leg at 4 years, right femur at 6 years, left femur at 7 years. On examination at the age of 7½ years she was 3 cm. below average height for her age and 3 kg. above average weight. The lower extremities were deformed at several sites. Roentgen examination disclosed narrow shafts in the long bones with rarefaction of the entire skeleton; the callus surrounding the most recent fracture was normally dense. The serum calcium concentration was 8.2 mg. per 100 c.c., the inorganic phosphorus 6.3 mg.

Additional observations may be summarized as follows: Nov. 16 to Dec. 20, 1937, 22 c.c. Praedyn were given intramuscularly, desiccated thymus by mouth. Dec. 29, 1937, patient had fracture of the left leg, greenstick type. Feb. 2, 1938, serum calcium, 9.4 mg. per 100 c.c. Praedyn was then given by mouth. March 18 to April 28, 1938, Pregnyl, 4,000 I. U., was administered intramuscularly; October, 1938, Pregnyl, 5,000 I. U., again administered intramuscularly. March 16, 1939, the height of patient was 6 cm. below average for age, weight, 1 kg. above average, and roentgenogram of the spine showed marked kyphosis at the thoracic level. March 16 to April 24, 1939: Pregnyl, 5,000 I. U., was administered intramuscularly and concentrated cod-liver oil and calcium were given by mouth; the patient complained of pain in the spine. On Sept. 11, 1939, roentgenogram of the spine showed osteoporosis. Dec. 28, 1939, to Jan. 29, 1940, Oestropur, 100,000 units, was given intramuscularly and Thyreoidin was given by mouth. On Feb. 1, 1940, a roentgenogram of spine showed considerable deficiency of calcium and concavity of the margins of the vertebral bodies. March 11, 1940, the height was 10 cm. below normal for age and weight 5.5 kg. above normal. Nov. 17, 1941, the serum calcium was 11 mg. per 100 c.c.; inorganic phosphorus, 3.7 mg.; phosphoric acid was administered by mouth. The tympanic membranes were blue-gray in color.

CASE 4.—I. G., younger brother of S. G., Case 3, was born April 4, 1931. He sustained a fracture of one femur when 14 days old and a fracture of the forearm when 9 years old. He had other symptoms, sclerae were blue and tympanic membranes were blue-gray.

S. G., Case 3, represents a typical example of the Lobstein syndrome. The value of her serum calcium, however, was subnormal when first measured; not until she was 11½ years of age did it reach normal level. The serum inorganic phosphorus was at first elevated, later normal, or slightly below normal. It is interesting to note that in the three typical Lobstein cases reported by Funk[2] an elevated level of serum inorganic phosphorus was likewise found. On the other hand, the typical Vrolik case cited by Fleming, Radasch, and Williams[4] showed at first a serum inorganic phosphorus concentration of 3.4 mg. per 100 c.c.; not until later did it rise to 5.8 mg.

The features on which Glanzmann[1] bases a differentiation between osteogenesis imperfecta (Vrolik) and osteopsathyrosis (Lobstein) are thus at variance with the clinical findings I have recorded. In our own experience Vrolik cases are found in Lobstein families. We also find that the values of serum calcium and inorganic phosphorus fluctuate in the course of the disease and fail to form the basis of a distinction between the two types. Contrary to Glanzmann's opinion, borderline cases occur which show elements of the two conditions.

However, the final judgment as to whether these diverse syndromes are of dual or of single origin depends in the last analysis on an elucida-

tion of their pathogenesis, which thus far remains a matter of conjecture.

CASE 5.—M. S., an only child born May 21, 1939, was admitted on May 18, 1943, at 5 years of age. There was no family history of hereditary illness. His development had been normal until March, 1941, when he had fever, became temporarily blind, and showed stiffness of the extremities. *Eberthella typhosa* was isolated from his cerebrospinal fluid. He recovered from this episode of meningitis but sustained fractures of the thigh 3½ and 6 months later. Bossing of the chest was first noticed one year prior to admission. His height was 16 centimeters below average for his age, weight normal for his height. His gait was waddling, with everted feet. He was able to rise from a supine to a sitting position only by grasping his lower extremities. The cranium had a maximal circumference of 49.5 centimeters;

Fig. 1.—Right femur (Case 5), lateral and anteroposterior views, showing callus and angulation deformity from old fracture between upper and middle thirds of shaft.

prominent parietal bosses were present, and a cracked-pot sound was easily elicited on tapping the skull. His sternum was bent forward, forming a right angle, and the spine showed a fixed kyphosis in the thoracic region; the circumference of the chest was 57 cm. The extremities were straight and slender. The eyes showed no bluish discoloration of the sclerae. Urinalysis and blood count were not remarkable. Serum inorganic phosphate concentration was 4 mg. of phosphorus per 100 c.c.; phosphatase 4 Bodansky units. Roentgenograms of the skeleton showed a deficiency of calcium throughout; the long bones were slender, with thin cortices, and healed fractures were seen in each femur with moderate callus formation (Fig. 1). The ribs were deformed, and the bodies of the vertebrae biconcave in outline

Fig. 2.—Lateral view of spine (Case 5), showing "fishtail" outline of vertebral bodies.

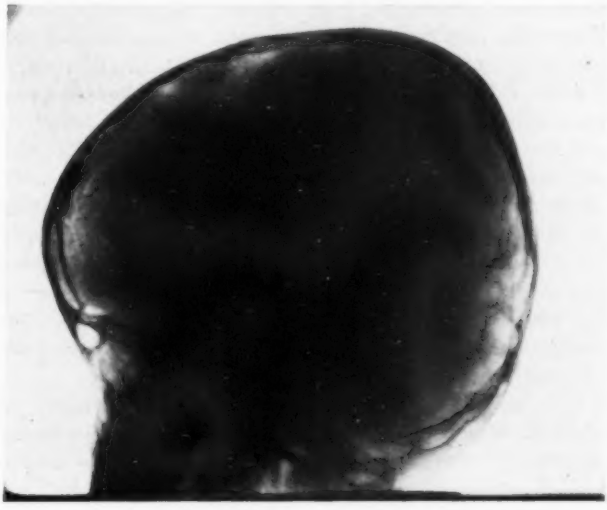

Fig. 3.—Lateral view of skull (Case 5).

(Fig. 2); several of the vertebrae exhibited marginal proliferation. The cranial plates were thin, with distinct increase in the digital markings (Fig. 3).

In this case, a male child who at the age of 22 months suffered from a typhoidal meningoencephalitis subsequently exhibited the clinical picture of osteopsathyrosis with decalcification of the skeleton, fractures of the femora, and deformities of the ribs and vertebral bodies. On roentgen examination of the cranium, signs of increased intracranial pressure were found.

Zondek[5] and later Liehtwitz[6] were the first to point out the pathogenetic relationship between cerebral disease and osteoporosis. Both of these authors place the site of the primary disorder in either the infundibular region or the hypophysis, and both describe osteosclerotic as well as osteoporotic alterations of the skeleton. In our Case 5 likewise, osteosclerotic changes developed, that is, osseous marginal proliferations in the vertebral bodies. A framelike thickening of the outlines of the vertebrae is described by Sehmorl and Junghanns[7] in cases of osteitis deformans (Paget) and of osteitis fibrosa generalisata. So far as we have been able to determine, our Case 5 represents the first instance of this marginal alteration of the vertebrae in association with osteopsathyrosis. It may be postulated that the body attempts in this manner to reinforce by compensatory formation of new bone the inadequate carrying power of the calcium-deficient vertebrae.

As in the cases described by Zondek and Lichtwitz, Case 5 exhibited decalcification of the skeleton following a cerebral disorder. Yet our patient was exceptional in that, in place of showing partial or temporary osteoporosis, he eventually displayed a condition corresponding to an acute, generalized, progressive, nonhereditary osteopsathyrosis.

It is noteworthy that Meissner[8] mentioned the occurrence of precocious puberty in a girl of 9 years suffering from osteopsathyrosis; he also described virile hirsutism in a girl of 17 years who likewise was affected by the same abnormality of the skeleton. Hagenbach[9] found excessive generalized atrophy of the spongiosa and reduction in size of the cortex of the long bones in a woman of 45 years who had a hypophyseal tumor.

With these facts in mind, the idea suggests itself that an alteration in the region of the hypophysis or infundibulum may provisionally be regarded as the origin of the skeletal abnormality both in typical cases of osteopsathyrosis (Lobstein) and in osteogenesis imperfecta (Vrolik). Consonant with this hypothesis is the well-known circumstance that fresh spontaneous fractures do not occur in osteopsathyrosis after puberty has set in.

Acting on this theory, I have for some years treated cases of osteopsathyrosis with extracts of anterior pituitary. The results have been encouraging. In the case of S. G. (Case 3) there occurred one spontaneous fracture immediately following the first series of injections, but during the next six years the patient remained free from further fractures. All other patients similarly treated showed no additional

spontaneous fractures, in spite of the fact that roentgenograms failed to demonstrate a restoration of normal osseous structure. Low dosage of endocrine preparations was employed in order to avoid premature precipitation of pubertal changes. It may well be that with higher dosage or with more persistent treatment the normal anatomic pattern of bone might be entirely restored. In any event, one may point out that abnormal concentrations of serum calcium and phosphatase disappeared following treatment with extract of anterior hypophysis (especially Case 3). Admittedly, biochemical changes of this kind may occur spontaneously in the course of a prolonged illness.

SUMMARY

1. Osteogenesis imperfecta of the Vrolik type and osteopsathyrosis of the Lobstein type appear to have a common pathogenesis and to represent different manifestations of a single disease.

2. Osteopsathyrosis may develop after cerebral disorders and presumably in response to them.

3. Osteosclerotic proliferation of the margins of the vertebral bodies has been observed in a case of osteopsathyrosis.

4. Treatment of osteopsathyrosis with extract of anterior hypophysis is recommended.

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AN EXAMINATION OF THE DEVELOPMENT OF CERTAIN ADAPTIVE BEHAVIOR PATTERNS IN INFANTS

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THE purpose of this study was to gather precise data on the development of certain adaptive behavior patterns in infants with the hope that, by a sifting process, those patterns which manifest a critical change at certain times in the infant's life might be selected as indices of normal development.

Extensive lists of the acts which the infant performs at different ages are available, but these are not very precise for the very early weeks of life. Besides, we have little knowledge of the relative value of the different items on such a behavior list. In this study the attempt was made to make a critical evaluation of a few patterns which seemed to have some diagnostic significance.

The selection of items for detailed examination was made from observations and cross-sectional studies of thirty-two different activities in infants at The Cradle in Evanston. Only those were selected which seemed to show some consistent relation to chronologic age.

Since the infants are kept at The Cradle for a period of ninety days, it was planned to make frequent observations of a number of infants throughout their entire stay. Eighteen infants were studied in this manner and the results are reported in this paper.

DESCRIPTION OF EXAMINATION METHODS

Great care was taken to obtain the responses of the infant under uniform conditions in order that the same observations could be made by any person who follows the same procedures.

The Cradle has three units, each unit comprising twelve cubicles. Each infant is kept for his entire stay at The Cradle in his own cubicle and ordinarily sees no one except the nurses and physicians. In this case, the psychologist became an addition to his social circle. No one is ever permitted to come into the unit where the infants are kept unless he is wearing a gown and a mask. In other words, the child never sees anyone who is not dressed in this standard manner and never sees any part of the face uncovered except the eyes above the level of the mask.

All observations were made after the infant had been fed and dried. Since the work in each unit was arranged by the nurses, the examiner timed her observations with the feeding schedules. The infant was

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fed by one nurse, was diapered by a second nurse, and then the psychologist came into the cubicle to make her observations and tests.

The detailed procedure was as follows:

I. Reactions to persons

The child must be lying on his back, fed, dried, and contented.

A. Kinds of social stimulation

Different social stimulations were given to the child as follows:

1. Watching the child

The examiner approached the crib, stood beside the child, and looked at him but made no sound nor any movement. The entire period of stimulation normally consumed about fifteen seconds.

2. Talking to the child

The examiner approached the child in much the same manner as in watching the child, but this time speaking to him in such a way that there was animation in her voice, just as a person would speak who was talking to a child who could understand. In order to standardize the content of the speaking, the examiner said: "Hello, (child's name). Here's a little poem for you." After this she recited in a conversational tone the whole six stanzas of "Mary Had a Little Lamb."

3. Playing with the child

The examiner talked to the child, picked him up, hugged him to her, cooed to him, and played in a manner similar to the way in which a mother plays with her child.

B. Kinds of responses

The responses of the infant were recorded according to the following four criteria:

1. No response

This was recorded when the infant gave no signs at all of being aware of the examiner's presence.

2. Passive attention

Any mild act of attention was recorded as passive attention. This included such things as looking at the examiner, making small responsive movements with his arms or legs, or turning his eyes to follow to a minor degree.

3. Active attention

This was recorded when the child smiled, cooed, laughed aloud, waved his arms or legs in an excited manner while looking at the examiner, or made any response which indicated obvious pleasure in the situation.

II. Visual fixation and following

A. The visual stimulus which was used throughout this test was a red, white, and blue pin wheel about six inches in diameter. The child was placed on his back and the pin wheel was held about fourteen inches from his face. Fixation is determined by a slight movement of the pin wheel to see whether there is a slight movement of the child's eyes.

1. Horizontal following

When the examiner is sure that the baby has focused and fixated his vision on the pin wheel, she moves the pin wheel slowly from one side of the crib to the other. This movement does not form an arc over the baby's face but is on a horizontal plane. The length of the movement is about twelve inches, that is, about six inches to each side of the median plane. This sidewise movement is repeated three times.

2. Vertical following

The same method is used in moving the pin wheel in a vertical manner. When making the vertical movement, the center of oscillation is determined

by the point where the child's eyes naturally fall. Again there are three backward and forward movements.

3. Circular following

Finally, the examiner moves the pin wheel in such a manner as to make three complete circles with a radius of six inches on the same horizontal plane, the center of the circle being the point of easy fixation for the child.

B. The records of responses are made as follows:

1. Does not fixate

If the child cannot be made to fixate after a period of approximately sixty seconds, the examination is discontinued and this fact recorded.

2. Fixates

This is recorded when the child definitely fixates.

3. Follows horizontally
   (a) Short distance
   (b) All the way and reverses
   (c) Continuously

This final record is given only when the child follows continuously as the pin wheel is moved from side to side.

4. Follows vertically
   (a) Short distance
   (b) All the way and reverses
   (c) Continuously

5. Follows circularly
   (a) Short distance
   (b) All the way

This is the recording when the child follows three complete circles but intermittently loses sight of the pin wheel.

   (c) Unbroken

III. Follows moving person

The examiner moves backward and forward along the side of the crib five times in easy sight of the child and observes whether the child follows these movements with his eyes. The scoring is done as follows:

(a) No following
(b) Short distance
(c) Backward and forward some
(d) Continuously

IV. Smiling and cooing

In addition to the above, records were made of whether the child smiled or cooed at any time.

RESULTS

This study represents approximately 5,300 observations made under uniform conditions and recorded with as much objectivity as possible. Each of the curves to be presented is the composite of between 400 and 600 observations.

We believe, also, that the reliability and validity of these observations is increased because the infants were observed in their normal surroundings with practically no disruption of their living routine. It is well-known that infants are easily disturbed and that their behavior under such circumstances is likely to be totally unrepresentative of their customary reactions. This feature of the experiment is

made possible by the almost ideal opportunity furnished by The Cradle for such work. Usually an infant is removed from the hospital at about 2 weeks of age and taken to his home. If the child is brought from the home to a psychologic laboratory for study, his routine is interrupted; whereas, if the psychologist visits the home, there would still be uncontrollable disturbances. At The Cradle, the opportunity was offered for continuous observation over a three months' period of the same child with no modifications of his mode of living.

It may be that the observations of the social reactions of these infants is not strictly comparable with similar records made with the entire face of the examiner exposed. However, we believe that the infant gave a more normal reaction to a customary experience than he would have done had we taken off the mask during our study. Even if this factor is given full weight in considering our results, the only curve which would be affected would be the one in which the infant's reactions to "watching the child" are reported. The rest are not affected by the personal appearance of the examiner.

The curves were constructed as follows:

For each five-day period the percentage of infants who manifested the type of behavior to be used in a specific curve was computed. Since this made a rather jagged curve in some instances, the running average of these percentages was used to smooth the curves. It was decided to locate as the critical value on each curve that point where 75 per cent of the observations indicated success in the task represented by that curve.

1. *Fixation.*—From the youngest age group the ability to fixate on the pin wheel exceeded our criterion test. By the age of 50 days, infants are able to fixate practically invariably; but over 75 per cent can fixate from the second 5-day period. This is shown in Fig. 1.

2. *Horizontal Following.*—The curves for the three degrees of horizontal following are shown in Fig. 1. Seventy-five per cent can follow a short distance at the 11- to 15-day age level; in following all the way and reversing, the 75 per cent criterion is passed at the 36- to 40-day level; and continuous horizontal following passes the critical point at the 46- to 50-day interval.

3. *Vertical Following.*—Vertical following proves to be just a little more difficult than horizontal following. Using the same criterion of 75 per cent, the critical point for following a short distance is 21 to 25 days, for all the way and reversing it is 36 to 40 days, and for continuous vertical following it is 51 to 55 days. These records are shown in Fig. 2.

4. *Circular Following.*—Circular following is still more difficult and indicates more maturity than either horizontal or vertical following. For following circularly a short distance the critical point is 31 to 35 days, for following all the way round it is 51 to 55 days, and for un-

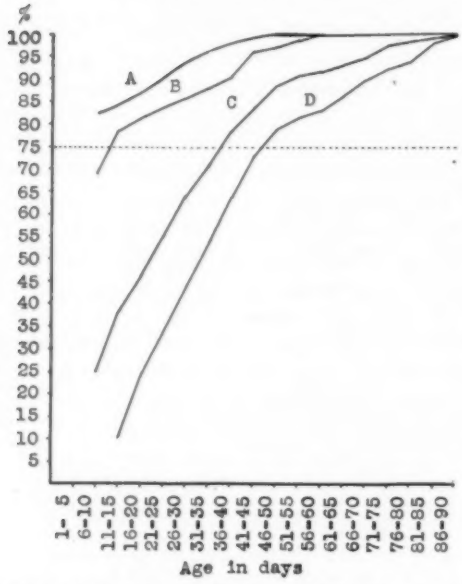

Fig. 1.—Fixation and horizontal following. *A*, Fixation curve indicates that infants passed the 75 per cent criterion mark in less than ten days of life. *B*, Horizontal following a short distance. *C*, Horizontal following all the way and reverse. *D*, Continuous horizontal following.

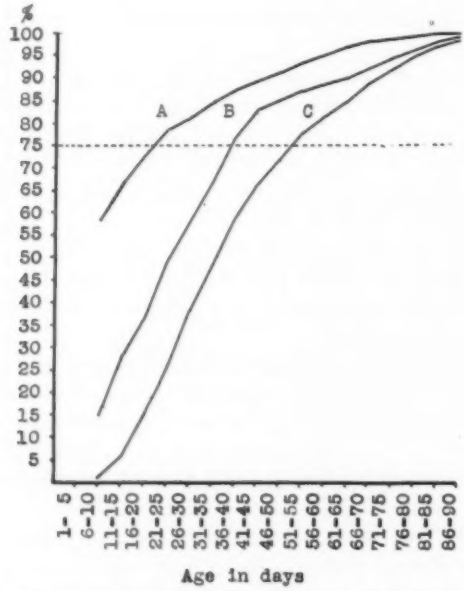

Fig. 2.—Vertical following. *A*, Vertical following a short distance. *B*, Vertical following all the way and reverse. *C*, Continuous vertical following.

broken circular following it is 71 to 75 days. These curves are shown in Fig. 3.

5. *Following Moving Person.*—In Fig. 4 are given the curves for the infant's ability to follow a person as she moves along the side of his bed. The critical point for following a short distance is 36 to 40 days, for following backward and forward some it is 46 to 50 days, and for continuous following it is 61 to 65 days.

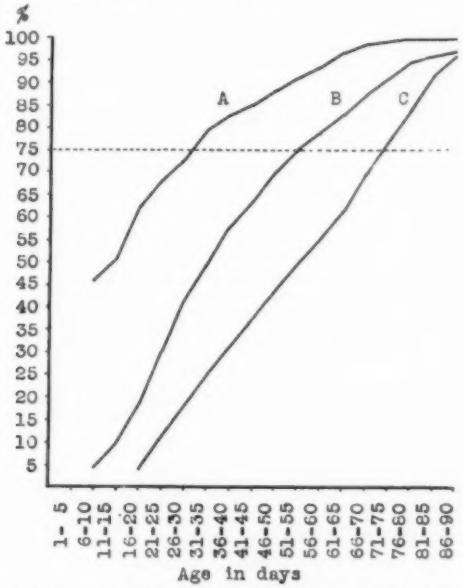

Fig. 3.—Circular following. *A*, Circular following short distance. *B*, Circular following all the way. *C*, Unbroken circular following.

6. *Reactions of the Child to Watching by the Examiner.*—In Fig. 5 there are two curves based on the infant's reaction to the visual regard by the examiner. The first is the curve for passive attention and has a critical point at the 26- to 30-day period. Active attention passes the critical point at the 66- to 70-day period.

7. *Reactions to Talking by the Examiner.*—In Fig. 6 two curves are given to show passive and active attention to talking by the examiner. Passive attention passes the critical point in the 31- to 35-day period. Active attention to talking passes the critical point in the 66- to 70-day period.

This finding presents an unexpected feature. One might presume that talking to an infant would be a more exciting stimulus than visual regard. This does not seem to be so. At least in the early stages the child is more likely to give passive attention to a quiet look than he is to the voice of the examiner. Active attention does not show this same differentiation.

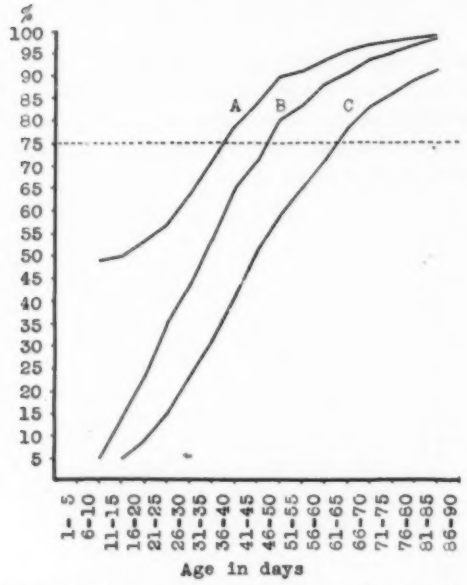

Fig. 4.—Following moving person. *A*, Follows moving person short distance. *B*, Follows moving person backward and forward some. *C*, Continuous following of moving person.

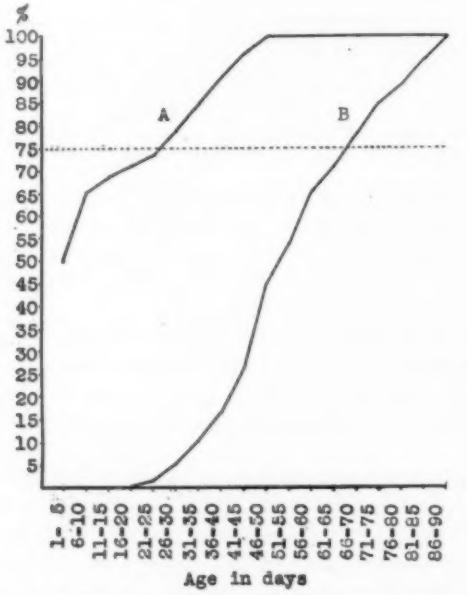

Fig. 5.—Reactions of infant to watching by examiner. *A*, Passive attention to watching. *B*, Active attention to watching.

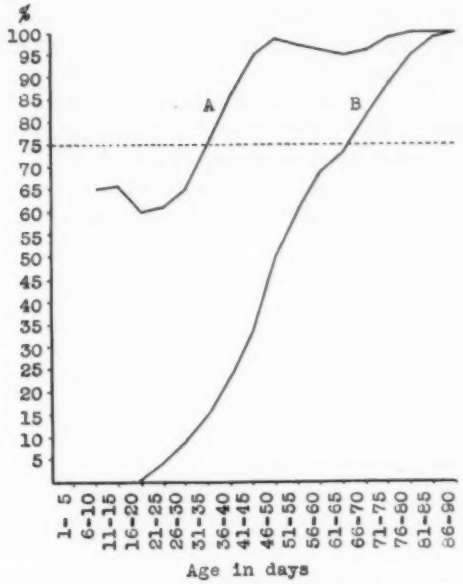

Fig. 6.—Reactions of infant to talking by examiner. *A*, Passive attention to talking. *B*, Active attention to talking.

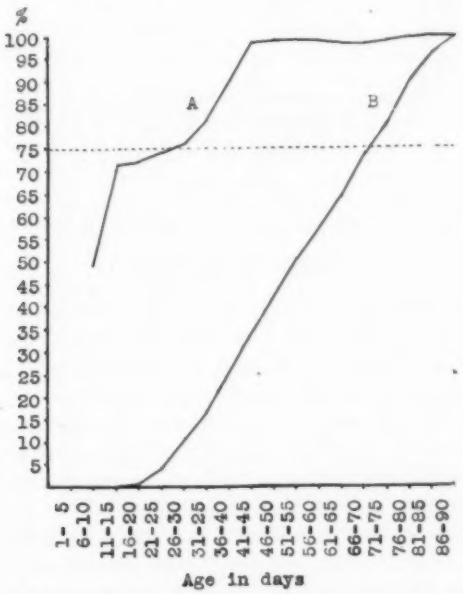

Fig. 7.—Reactions of infant to playing by examiner. *A*, Passive attention to playing *B*, Active attention to playing.

8. *Reactions to Playing With the Child.*—Fig. 7 shows that the infant gives passive attention to playful activities by the examiner at the 26- to 30-day period in 75 per cent of the observations and gives active attention in the 71- to 75-day period in a similar proportion of cases.

9. *Smiling and Cooing.*—The reactions of smiling and cooing are not very far apart, the cooing curve passing the critical area only ten days later than the smiling curve, as shown in Fig. 8. Smiling passes the critical area at the 56- to 60-day period and cooing at the 66- to 70-day period.

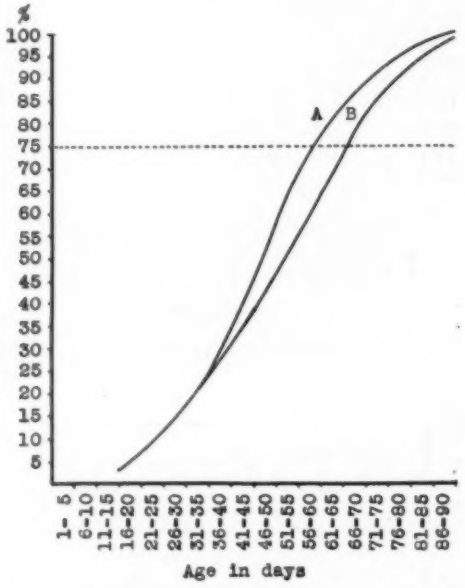

Fig. 8.—Smiling and cooing. *A*, Smiling. *B*, Cooing.

A BEHAVIOR SEQUENCE

The materials presented in Figs. 1 to 8 may be brought together in chronologic order as determined by the time when they pass the 75 per cent criterion (Table I). With this arrangement at hand, one can follow the progress of a child in order to study the degree to which he conforms to the sequences found in these Cradle infants. This developmental sequence is given only as a tentative picture of progress and with the reservation that it merely represents what was found with eighteen infants in a restricted environment. It would be a mistake to take these as well-established norms against which to measure any individual child. Furthermore, these results say nothing more than that these children passed through the designated stages. No assumptions are made as to the possible relation of such sequences to intelligence, future progress, or educational fitness.

TABLE I

DEVELOPMENTAL SCALE

AGE OF INFANT (DAYS)	REACTION PATTERN	FIG.
1 to 10	Fixates	1
11 to 15	Follows horizontally short distance	1
21 to 25	Follows vertically short distance	2
26 to 30	Passive attention to visual regard	5
26 to 30	Passive attention to playing	7
31 to 35	Follows circularly short distance	3
31 to 35	Passive attention to talking	6
36 to 40	Follows horizontally all the way and reverse	1
36 to 40	Follows vertically all the way and reverse	2
36 to 40	Follows moving person short distance	4
46 to 50	Follows horizontally continuously	1
46 to 50	Follows moving person backward and forward some	4
51 to 55	Follows vertically continuously	2
51 to 55	Follows circularly all the way	3
56 to 60	Smiles to examiner	8
61 to 65	Follows moving person continuously	4
66 to 70	Active attention to visual regard	5
66 to 70	Active attention to talking	6
66 to 70	Cooing	8
71 to 75	Unbroken circular following	3
71 to 75	Active attention to playing by examiner	7

SUMMARY

Eighteen infants were studied at frequent intervals at The Cradle in Evanston throughout the first ninety days of their infancy. Careful records were made of their ability to follow a visual stimulus in a horizontal direction, in a vertical direction, and circularly and of their reactions to watching by the examiner, to being talked to and played with by the examiner, and of any smiling, or cooing.

The 5,300 observations thus procured were reduced to a percentage basis and smoothed curves constructed for each of the activities recorded. Using as a critical point the age at which 75 per cent of the observations showed successful performance, a developmental scale was devised in which critical points extend from the first ten days of life to the 71- to 75-day period.

American Academy of Pediatrics

Proceedings

MEETING OF THE EXECUTIVE BOARD

CHICAGO, ILL., JUNE 10 TO 11, 1944

Report of Committees

Committee for Cooperation With Nonmedical Groups

First, I regret to state that our national committee has not functioned well during the last year, due largely to little or no direct contact with the state representatives. The last time I wrote to all of the state chairmen I heard from only a small number. A number of responses stated that the state chairman had entered the service and no substitute had been appointed. A number of reply letters stated that the usual activities were going on but that the pediatricians were so busy they could take on no extra work. I assumed a similar situation existed in the states from whose chairmen I did not receive a reply. I think it is quite obvious that the pediatricians have been working under great pressure the last year and a half in nearly every community. This undoubtedly explains the apathy of the state committee chairmen to the responsibilities of this committee.

The last time I heard from Mr. Rose of Mead Johnson & Co., I was told that there was a marked decrease in the number of requests for the film, "When Bobby Goes to School." This lack of interest in the film was shared by medical groups as well as lay groups. Fewer meetings, requests for nutrition programs, and other war activities account for this decline. I feel sure that renewed emphasis can be placed on this film when the demand from war activities can be relaxed.

Dr. Grulee recently sent me a report of the meeting of the Advisory Committee to the National Congress of Parents and Teachers. Dr. Joseph A. Johnston, a member of this committee, represented the Academy at this meeting. I am enclosing his report for your information. It appears that the present emphasis is being placed on the Emergency Maternity and Infant Care Program for the wives and infants of servicemen. Support of this program is not specifically a function of this committee for I believe that the Academy has a national committee that deals with governmental agencies. I know, however, that members of our national committee and in many states members of the state committee have cooperated with the official groups to aid in setting up this program and assist in its efficient operation.

The Nursery School program has been greatly expanded throughout our country during the last year. Again our committee has functioned mainly in an advisory capacity. Inasmuch as the funds for the conduct of these schools have been largely from federal grants they have been administered through state and local official organizations such as

Boards of Education, Welfare Departments, and State Health Departments. At the recent meeting of the American Public Health Association in New York City the war nursery schools were thoroughly discussed. I was present at this meeting and took part in the discussion. A number of Academy members were invited to participate in this round table discussion so that it was possible for us to exert some influence on the medical supervision of these schools. The regular nursery schools not supported by federal or state grants have inserted into their prospectus the statement prepared by our committee on the medical benefits of good nursery schools. A syllabus for nursery school teachers which our committee agreed to sponsor has not yet been completed. I had hoped to have it in your hands some time ago but for reasons over which I have no control it has not been completed. It was to have been well illustrated, but paper and other shortages may delay it indefinitely. Our relation with the National Group on Nursery School Education is a cordial one and here also I feel we will be called upon for more support when the emergency conditions no longer prevail.

Last year Mrs. May Dickinson Kimball of Boston, who is chairman of the Mothercraft Group sponsored by the General Federation of Women's Clubs of America, wrote me about the work done with young girls by this group throughout America. I was informed that two million young girls were enrolled in these clubs. Much of their teaching and training is along health lines. She invited me to prepare a radio talk to be used by all of the groups as part of their training this year. This talk on the health problems of high schools I prepared some months ago. It is being used along with others as part of their course this year. It is being given as a message from the American Academy of Pediatrics. I was asked to speak at their annual meeting in Boston this year but lately learned that the meeting had been indefinitely postponed. This group evidently has considerable influence with young girls, but like other organizations seems not to be functioning at full capacity now. However, it opens a new field for cooperation when the stress of war is over.

This is, I believe, the extent of official participation which our committee has had with groups engaged in child health activities.

As Chairman of your committee I feel rather uncertain as to what we should do this year. Wherever I meet pediatricians the problem is the same. The men have about all they can do to take care of the sick children and carry on such preventive work as they feel must be done in their own community. I have not attempted so far this year to contact the State Committee Chairmen. I will do so if you feel it is desirable. I would like your opinion as to what we should try to do during 1944. Are we falling down in our responsibilities and, if so, what things come first in the present war period?

ALBERT D. KAISER, Chairman

Committee on Governmental and Medical Agencies

Over a period of several years our committee developed a seven-point program dealing with the subject of how a State Academy Fellowship could be of constructive service to Better Child Health by various methods of cooperation with state, governmental, and medical agencies.

This program was developed with the able aid and assistance of the national officers and executive board of the Academy and Dr. Martha

Eliot, Associate Chief of the Children's Bureau, and her staff, and, when completed, receive the official approval of the Academy as a whole and has been of some service to the states. In many of our states there is wholehearted cooperation between the Bureau of Maternal and Child Health of the State Departments of Health and the State Medical Society and other medical agencies, which is assisted considerably by the cooperative aid of our State Academy Fellowships.

We wish it could be said that a similar cooperation exists at national level, but it is obvious that such is not the case.

The whole delicate fabric of the gradual development of Better Child Health, which our Academy Fellowship has been helping to weave through the years, seems likely to be ruined unless the differences of opinion and other difficulties attending the Children's Bureau Emergency Maternity Infancy Program and the Wagner-Murray-Dingell bill are composed by some democratic form of collaboration between governmental and medical agencies. If this can be done at state levels, which has been amply demonstrated, there seems no good reason why it cannot be done at national levels, providing good American democratic procedure is observed throughout, coupled with a considerable amount of good will and good faith on the part of the participants officially representing governmental and medical agencies.

Notwithstanding these temporary stalemates, which at present seem to block progress as to this necessary, wholehearted collaboration for Better Child Health in our national picture, we believe progress can be made in this direction by a *study* of the factors involved and subsequent recommendations made by our Academy to both governmental and medical agencies. We further believe that 80 to 90 per cent of the best Child Health brains in these United States are in the possession of outstanding Fellows of our Academy, and that the Academy has a job to do in this critical year of 1944.

This committee, therefore, is undertaking to study and develop a program on Cooperation with Governmental and Medical Agencies at a National Level to present to the executive board of the Academy at St. Louis in November, 1944. Realizing the need of the most able assistance procurable in making this study, we are requesting President Gengenbach to appoint as advisory members of this committee a number of Fellows, who have had wide experience as to Child Health in both governmental and medical agencies as well as in the Academy's past development. Among those requested are Drs. Joseph Wall, Oliver Stringfield, Borden Veeder, Josephine Baker, Ethel Dunham, Harrold Murray, Wilburt Davison, Albert Kaiser, Harold Mitchell and Leona Baumgartner and such of the national officers and executive board as might be able to meet with us at any of our meetings.

Our first meeting to study this problem will be held at 5 P.M., Wednesday, May 10, at the Hotel Pennsylvania, New York City, where several of the committee and advisory members will be attending the Annual Meeting of the New York State Medical Society. The committee will thereafter continue the study by correspondence or by meetings at New York or along the eastern seaboard. The final meeting on this problem will be held at St. Louis in November.

Suggestions and advice from interested Fellows will be appreciated as to this peculiarly difficult problem. Copies of the present state level program for study are available from the Chairman.

In spite of the great difficulties in the pediatric wartime practices of all of us, by this study the committee hopes to be able to submit to

the executive board in November a worth-while contribution to the real aims and objectives of the American Academy of Pediatrics.

October, 1941—Seven-Point Program of the American Academy of Pediatrics Committee on Cooperation With Governmental and Medical Agencies

1. ACADEMY RELATIONSHIP TO STATE MEDICAL SOCIETY

The chairman and his committee should devise some feasible method for assuming leadership of the Child Health policies in his State Medical Society. (It is suggested, where necessary, that effort be made to establish in each state and county Medical Society a Committee on Child Health, with adequate representation of Academy members.)

2. USE OF FELLOWS OF THE ACADEMY BY STATE MEDICAL SOCIETY

In collaboration with, and with the approval of the state chairman of the Academy, the state or province chairman of this subcommittee should annually address a letter to the president of the State Medical Society, enclosing a list of the Academy Fellowship of that state or province, and offer the services of the Fellowship to act as leader in all types of Child Health activities in his state or province.

3. USE OF FELLOWS IN THE COORDINATION OF CHILD HEALTH ACTIVITIES IN STATE DEPARTMENTS OF HEALTH AND STATE MEDICAL SOCIETIES

The chairman of the subcommittee should endeavor to coordinate the Child Health activities of the State Department of Health with that of the State Medical Society in his state or province.

4. USE OF FELLOWS OF THE ACADEMY BY STATE DEPARTMENTS OF HEALTH AND OTHER STATE PUBLIC AGENCIES

In collaboration with, and with the approval of the state chairman of the Academy, the state chairman of this subcommittee should annually address a letter to the Directors or Commissioners of the State Board of Health and other state public officials of agencies having to do with any phase of Child Health, volunteering the assistance of the Academy Fellowship in the carrying out of the Child Health phases of the state or province health program.

5. USE OF FELLOWS AS ADVISERS AND ON GOVERNING BOARDS OF STATE AGENCIES

The chairman of the subcommittee should recommend that Fellows act as Child Health Advisers to all official state agencies, having some phase of Child Health activities in their program, and also urge that Fellows be appointed to the governing bodies of such agencies.

6. DESIRABLE STANDARDS OF QUALIFICATIONS

The state chairman of this subcommittee should use its influence to promote, through joint action of the Child Health Committee of the State Medical Society and the Child Hygiene Division of the State Department of Health, the establishment and maintenance of desir-

able standards regarding qualifications of all official personnel in health departments, and to work for the adoption of Merit Systems in all states and their political subdivisions, in accordance with the standards established by national organizations in their respective fields.

7. RESPONSIBILITY AND PARTICIPATION IN ALL TYPES OF CHILD HEALTH SERVICE

The state chairman of this subcommittee shall endeavor, by every practicable means, to stimulate increased responsibility for, and increased participation in, all types of Child Health services, in their own community, in their own county and state, by every State Fellow of the American Academy of Pediatrics.

Note: Some types of Child Health services which particularly need increased integration of the Academy Fellowship:

1. Hospital ward service
2. Hospital clinic service
3. Public health conferences
4. Preschool and child health conferences
5. School health services
6. Child guidance and mental hygiene program
7. Adolescent hygiene programs
8. The pediatric part of tuberculosis case finding
9. Immunization clinics
10. The pediatric part of crippled children's clinics
11. The pediatric services involved in voluntary health insurance programs
12. The medical supervision of children's camps, etc.

In order to further state cooperation of governmental and medical agencies, whenever possible, the chairmen of the Child Health Committees of the State Medical Society (or the Public Health Committee if no Child Health Committee exists), and the Chief of the Maternal and Child Health Division of the State Health Department, should be appointed by the state subcommittee chairman of this committee to the subcommittee (for cooperation with governmental and medical agencies) in each state.

By the above methods each State Fellowship of the American Academy can act as the principal responsible advisory group for the State Departments of Health and other official state agencies, the State Medical Societies and the lay agencies having Child Health programs for the definite development of Better Child Health activities in each State.

STANLEY H. NICHOLS, Chairman

Committee on Pan-American Scholarships

I regret to report that during the year we lost one of the members of our committee, Dr. Fred Schlutz, who has been most active in the furtherance of better inter-American relationships. It will be difficult to get along without his help.

The committee suggests that among others Dr. McCune be considered for membership on this committee.

One member of the committee was present at the Second Mexican Congress for Pediatries and had an opportunity to discuss with a number of the Mexican members of the Academy our scholarship program. They were most enthusiastic about it and felt that it was giving the younger men a splendid opportunity to develop initiative to go out into cities that have no pediatricians at the present time.

We are happy to report that the difficulties that have been encountered by the institutions to which we had sent scholars have been entirely on the basis of an insufficient knowledge of the English language by the scholar. While in Mexico City, the member of the committee also had contact with Mr. Stevens of our embassy, in charge of the local Institute for Cultural Relationships, and it is hoped that through these institutions in the various Latin-American countries it will be possible to further control any language difficulty which these men may have.

I also wish to report that in a recent conference with Dr. Horning he expressed the pleasure and satisfaction of the Kellogg Foundation with the way the program is working out. The committee suggests that it would be fitting for the executive committee to send a formal expression of appreciation to the Foundation for their cooperation in making this program possible, as well as to the other sponsors of scholarships.

HENRY F. HELMHOLZ, Chairman

Committee on Geographical Distribution of Pediatricians

In answer to your letter of April 6, may I say that I am having inquiries relative to the geographical distribution of pediatricians and I am glad to offer such information as I have collected for the particular regions in question.

As soon as the present measles epidemic subsides I expect to resume the study of distribution and add to the material at hand.

This is as much as I have for my report at the present.

OTTO L. GOEHLE, Chairman

Report of the Committee on National Defense

The activities of the committee continue to be centered on the medical supervision of refugee children in cooperation with the United States Committee for the Care of European Children. Groups of physicians have been organized to examine and to provide medical care for these children at various Reception Centers before placement. Examinations have included Schick and Mantoux tests and chest x-rays of positive reactors. Not all physicians who gave their services were members of the Academy, but in all instances, the examinations and care have been most competent. Specialists were consulted whenever necessary. Services have always been on a voluntary basis and the spirit of cooperation has been excellent.

At intervals from April 1, 1943, to date, seven groups comprising eighty children were received in three centers located in Pleasantville, N. Y.; Bronx, N. Y.; and in Newark, N. J. In addition to the physicians mentioned in the last report who examined previous groups, the following assisted in this work: Drs. J. Hauser and Edison Shaw of Pleasantville, N. Y.; and Drs. Epstein, Schotland, Fine, Fost, and Kornfeld of Newark, N. J. Additional services were rendered by the Westchester County Board of Health, the Health Department of the City of New York, and the Beekman Hospital in New York City.

When Dr. Stimson relinquished the chairmanship of this committee, he suggested that additional activities might still be undertaken. In line with this thought the following items were submitted to Dr. Gengenbach for consideration: the day care of infants and children of servicemen's wives; postwar plans for adjusting adolescents to full-time or part-time high school studies after leaving profitable wartime occupations; investigation of residual detrimental effects on the health of the adolescent sustained in industry; and provision for short internships in approved hospitals for pediatricians who have been in the services for extended periods before resuming practice.

It was subsequently found that these projects were being considered in part or as a whole by other committees of the Academy or by organizations and agencies in the municipal, state, or federal governments. Because of its immediate urgency, one of these, the matter of child care centers, was explored more thoroughly. Interviews with the heads of several active groups in New York City revealed that facilities for the care of children with provisions for a wide range of services were already available, but these varied in degree in different sections of the community. It was obvious that in this project, the best results could be attained only by the coordination and perhaps consolidation of various committees and agencies dealing with the same problem. This integration of effort is particularly important both for the present emergency and for the future development of the nursery and child care centers. In the formulation of these plans it cannot be urged too strongly that members of the Academy be consulted for their experience and knowledge of children in particular areas, and for maintaining fundamental standards of health and sanitation in any centers that are established.

CARL H. SMITH, Chairman

Committee on School Health

I am sorry that I have no report for the committee on school health of the Academy. I had hoped that my plans would have developed enough to justify reporting. We are still concerned with the presentation to educators of the report on The Qualifications of School Physicians. The A.P.H.A. Committee on Professional Education is about to bring out a report on this subject and I am expecting that it will be altogether consistent with our report.* If so, we shall have their assistance in reaching the educators.

Another problem is concerned with the terms of employment of all part-time physicians working in the schools. There is a tremendous difference between the conditions of employment of such physicians. There are some schools that will have one physician for 10,000 children where they expect the impossible from him, and there are other schools where there is one physician for only 300 children and yet the administrators who hire these physicians are not aware of these extremely unusual conditions under which the physicians work. They may require the same amount of time for 300 children as for 10,000 children in another community. The reason the administrators are not aware of these

*The A.P.H.A. Committee report is consistent with our report except that they have left out of consideration the recommendations that we made concerning a medical advisory committee and the organization plan recommended to obtain sound decisions upon the selection of physicians for work in the schools. We shall continue to try to get over these ideas so that sound medical leadership may be available to the schools particularly where the control is now dominated by law educational authorities.

ridiculous differences is because there has, heretofore, been no common basis for reporting the time and work of the physician. It is this problem that I have been studying and hope that our committee may be able to make a report upon it later. This report, however, will not be worth much until we can make a proposal that will be likely to be acceptable to those administrators who employ physicians in the schools.

HAROLD H. MITCHELL, Chairman

Special Committee on Rheumatic Fever

Following the Conference on Rheumatic Fever held in Washington, D. C., on Oct. 5 to 7, 1943, under the direction of the Children's Bureau, the Committee on Rheumatic Fever submitted a report. This was published in the JOURNAL and is now a matter of record.

Following this, a number of the committee met on Jan. 26 to 27, 1944, in New York City, at the invitation of the American Heart Association. At this meeting the Council on Rheumatic Fever was formed representing a number of groups interested in the rheumatic fever problem. A report of this Conference has been submitted to the JOURNAL for publication at an early date with simultaneous release to be made in a number of other medical journals.

A report on the activities of the committee has been sent for inclusion in the booklet for state chairmen. With seventeen state programs now in operation, the committee is of the opinion that the Academy can play an increasingly important role in the development of these programs. It is to this end that the committee has directed itself.

ALEXANDER T. MARTIN, Chairman

Report of the Delegate of the American Academy of Pediatrics to the Second Congress on Pediatrics held in Mexico City, D. F., March 26, to April 1, 1944

By direction of the Executive Board, I attended the Congress as the official representative of the Academy. The United States had as additional visitors, Drs. Henry F. Helmholz, Bela Schick, Irvine McQuarrie, Archibald Hoyne, and Henry Gerstenberger, all members of the Academy and all of whom presented papers before the scientific sessions.

There were three sessions each day beginning at 10:00 A.M., with luncheon to which all the registrants were invited. These daily luncheons held on the spacious grounds of the new Children's Hospital proved the medium for delightful social contacts with the Mexican physicians and guests who numbered almost four hundred.

The officers of the Congress were Drs. Mario Torroella, president; Federico Gomez and Rigoberto Aguilar, vice-presidents; Hermilo L. Castaneda and Raphael Soto, secretaries-general; Augustín Navarro, treasurer. All of the above-named, with the exception of President Torroella, are Fellows of the American Academy of Pediatrics.

Aside from the plenary sessions of the Congress, there were section meetings on medicine, surgery, ophthalmology, orthopedics, the hygiene and nutrition of infancy, poliomyelitis, and others. Through the courtesy of the Mexican pediatricians, the North American representatives were frequently invited to preside at these meetings. The evening sessions consisted largely of presentations of papers by visitors including our Fellows of the Academy.

The interest of the Mexican pediatricians first aroused by the successful "mission to Mexico" of the secretary-treasurer, two years ago, was everywhere apparent. It was abundantly evident that these alert, intelligent physicians were proud of their association with the Academy made possible largely through the exertions of Dr. Grulee, and many of them expressed the hope that they might be able to attend the Annual Meeting to be held in St. Louis in November. If assurance of such attendance should be forthcoming, it might be a gracious gesture of the program committee to include in its panels some of our Fellows from Mexico whose experiences, especially with tropical diseases and deficiency states would be a distinct contribution.

Of especial moment and interest should be noted a meeting held on the afternoon of Friday, March 31, in the auditorium of the Nurses' Home of the Hospital Infantil, for the purpose of conferring certificates of Fellowship upon the fifteen Fellows residing in Mexico.

This proved to be a very delightful occasion and was attended by all but one of the Fellows, each being called to the stage to receive from the vice-president of the Academy his certificate of membership with a handshake of congratulation. Dr. Jorge Munos Turnbull, a visitor to the Eighth Pan American Congress held in the United States a few years ago, whom many will remember, was prevented from attending owing to a hospital emergency but later received his certificate and felicitations from your delegate.

Appropriate remarks were made by the writer, by Dr. Henry Helmholz, and by Dr. Raphael Soto. All of the visitors from the United States were present at the ceremonies. I feel assured that the presence at the Congress of an official representative of the Academy together with the attendance and participation of the other fellows of the Academy previously noted, accomplished much in furthering the interest and good will of our new members in Mexico in the affairs of the Academy.

We have taken the liberty to attach to and make a part of this report a brief summary of the Congress written for *The Children's Hospital Arrow* of Washington in answer to many requests for information from members of the Academy residing there.

Respectfully submitted,

JOSEPH S. WALL

THE SECOND MEXICAN CONGRESS OF PEDIATRICS*

The Congress was officially opened on the morning of March 26, 1944, by the President of the Republic, General Manuel Avila Camacho, and continued its sessions throughout the entire week, with meetings morning, afternoon, and evening. About four hundred physicians registered, including representatives from nearly all of the Central American countries and Cuba. Five Fellows of the American Academy of Pediatrics, with the Vice-President as the official delegate, took part in the sessions, several of which included scientific papers presented by the visitors from the United States. The Children's Bureau of the U. S. Department of Labor had as its official delegate Mrs. Elizabeth S. Enochs.

Judging by the enthusiasm displayed by those in attendance upon the Congress, there has been a renaissance in pediatrics during recent years throughout Mexico and her sister republics; nor is it improbable that the influence of the United States has had a marked bearing upon this rebirth of interest in the welfare of children. Of the six highest ranking officers of the Congress, five are Fellows of the Academy of Pediatrics, which also includes in its membership the Director of the new Mexico City Children's Hospital.

*From *The Children's Hospital Arrow*, Washington, D. C.

On the staff of this new hospital there are many pediatricians who received post-graduate training in hospitals throughout North America, under the aegis of scholarships provided by the Academy of Pediatrics and the Pan-American Union. This tendency of the younger Spanish-American physicians to further their pediatric education by courses of study in the States has been noted in our own Hospital for over a decade, during which time we have rarely had a resident staff which did not contain one or more physicians from lands south of the border. During the past winter, there were four Spanish-speaking residents serving the Hospital in the capacity of Residents or Fellows.

The visitor to Mexico, as he looks from the windows of the train winding its leisurely way southward through the cactus-covered plains, is struck by the evidences of the need for pediatric and social interest in behalf of the children. The train stop at each little adobe-hut village is the event of the day, for from every doorway emerge men, women and children—especially the latter. Nearly every woman carries a baby in her arms, or safely ensconced in a shawl, ingeniously wrapped about mother and child to form a snuggle-bunny, so that the mother's arms are left free for her other duties. The older children wear clothing so tattered and torn that it would fall apart of its own volition but for the skillful needlework of the mother who, by the use of patches of varied hue and size, has made serviceable for her offspring a garment which closely resembles grandmother's heirloom bed quilt.

Malnutrition is strikingly evident, and tuberculosis still the leading plague of the young. Aside from maternal nursing, which fortunately has not passed out of vogue in Mexico, the problem of securing proper and sufficient food for the rural children is an enormous one. There are but few cows to be seen, probably because of the utter lack of pasturage during the long dry season; but fortunately for the babies, goats seem to be fairly plentiful. A few years ago it is said that a prominent pediatrician wanted a law passed to forbid the feeding of milk to babies because of its impurity. It is also said by those who should know, that the diet of children after weaning consists mostly of cornmeal products. This is often supplemented by liberal doses of "pulque," an alcoholic drink made from the agave plant, and somewhat akin to the "moonshine" of the States.

A word of praise should be said for the somewhat socialistic government of Mexico, which has, in recent years, attempted much to alleviate the condition of children throughout the country; more especially to extend education help through the establishment of innumerable Federal Schools, whose attractive Spanish architecture looms strikingly amidst the squalor of the clustering adobe huts. Within the larger cities the government has established many modern child welfare centers which are staffed by young pediatricians and are accomplishing much good. There are sixteen such maternal and child health centers in Mexico City. The one visited by the writer was conducted in a most efficient manner by a group of physicians, nurses and social workers whose technic of examination, of keen interest in their clients, and of meticulous oral and printed instruction to the attending mothers, appeared above reproach. It was interesting, although unfortunate, to read on many of the social history notes that the father of the family made a daily wage of from two to four pesos (forty to fifty cents).

The modern center we visited had within its walls the usual Spanish patio with an attractive garden in which the runabout children of working mothers were cared for. They were given breakfast, dinner and supper before being called for at the close of the day.

By far the greatest contribution of the government to the welfare of children was the opening just a year ago in Mexico City of the New Children's Hospital which was built at a cost of a million and a half dollars. The façade of this concrete and steel building occupies nearly a city block, while to the south extend six wings, each of which terminates in a solarium open to the cloudless Mexican skies. No drop of rain falls during the several months of the dry season, and even in the wet season, according to my Mexican informants, the hand of nature is kindly, inasmuch as the torrential rains begin promptly at one o'clock, ending an hour later—always with such punctuality that watches may be actually set by "rain time"!

The Hospital Infantil is equipped throughout with every modern device and appliance of benefit to the sick children. The wards are all cubicled and parents view their children through glass windows without entering the wards. The operating rooms are especially intriguing. Students and observers must ascend to a second floor room directly above the operating field but are completely isolated from the scene of operation by a glass dome through which they may look down upon the surgical staff at work. The operating surgeon talks to his observers through a microphone connected with the isolated glass room by loud speakers.

The Director of the Hospital Infantil, Dr. Federico Gomez, together with several of his associate pediatricians, have had post-graduate training in the United States, and it was interesting to renew acquaintance with many members of the Staff who had visited our own Hospital upon the occasion of the clinic and luncheon we extended to the delegates of the Eighth Pan-American Congress on Pediatrics two years ago.

The sessions of the Congress were held in the auditorium of a new building not quite completed, the Institute of Cardiology, which was recently dedicated. Passing in and out to the meetings, we were fortunate to see Mexico's greatest and most outspoken painter, Diego Rivera, hard at work on the murals adorning the lobby. It was a relief from the tedium of listening to lengthy medical dissertations, to look over the shoulders of this artist while his quick, facile brush delineated the history of cardiology from primitive Indian times, when the medicine men of Mexico injected their remedies through the veins by means of a puncture made by an arrowhead.

The courtesy and hospitality of the Spanish physicians was delightful. Their wives were equally anxious to provide entertainment for the visitors. During the week of the Congress it is certain that no "siestas" were taken by either hosts or visitors. It may have been the high altitude or the Mexican air, but whatever it was, the idea of the necessity for sleep was banished for the duration of the Congress, and nearly every evening we were invited to the charming homes of our hosts to share therein a cordiality of welcome which has left lasting memories.

JOSEPH S. WALL

The Pediatrician and the War

Dr. Katharine G. Dodge of New York is in the U. S. Public Health Service, Office of Foreign Relief.

Dr. Hulda E. Thelander of San Francisco has been commissioned Lieutenant Commander in the Navy and assigned to the Marine Corps.

Dr. Herbert C. Archibald of Oakland, Calif., and Dr. Frank X. Guistra of Brooklyn, N. Y., have been commissioned First Lieutenants in the Army Medical Corps.

Dr. Henry C. Niblack of Chicago has been commissioned Major in the United Nations Relief and Rehabilitation Administration.

The following Fellows of the *American Academy of Pediatrics* have been promoted:

Captain Louis Appel, Flushing, N. Y., to Major.

Lieutenant Joseph Davis, San Francisco, Calif., to Captain.

The following Fellows who were admitted to membership in the Academy in June are in service:

Army

Albert A. Frank, Malden, Mass. (Captain)
Joseph M. Klein, Wilkes-Barre, Pa. (Lieutenant)
Samuel Jacob Werlin, Troy, N. Y. (First Lieutenant)
Warren F. Welknap, Detroit, Mich. (Captain)
Alexander N. Freed, Cleveland, Ohio (Captain)
Richard J. Lien, Rochester, Minn. (Captain)
Henry Siegel, Detroit, Michigan (Major)
George E. Stafford, Salina, Kansas (Captain)
George H. Wegmann, Milwaukee, Wis. (Captain)
Carl Witus, Detroit, Michigan (Captain)

Navy

A. S. Hurt, Jr., Richmond, Va. (Lieutenant Commander)
Milton Kurzrok, Brooklyn, N. Y. (Lieutenant Commander)

If Your Baby Must Travel in War Time. Bureau of Publications 307, Children's Bureau, Washington, 25, D. C. Supt. of Documents, Government Printing Office. Illustrated by Gluyas Williams, price, 5 cents.

This is a most welcome and timely little pocket size pamphlet with sound and sensible advice for mothers traveling with babies on trains, coaches, etc. This problem of travel is one faced by all pediatricians and they will render a great service by putting this little pamphlet in the hands of parents who feel they must travel with their babies and children during these days.

News and Notes

Dr. Joseph Brennemann died at his home in Reading, Vt., July 2, 1944. He was 71 years of age. Dr. Brennemann was one of the outstanding clinicians and teachers in American pediatrics. From 1921 to 1941 he was Chief of Staff of the Children's Memorial Hospital in Chicago, and Professor of Pediatrics at the University of Chicago School of Medicine. From 1941 to his retirement last year he served as Chief of Staff at the Children's Hospital in Los Angeles and as professor of pediatrics at the University of Southern California School of Medicine. He was Editor of "Brennemann's Practice of Pediatrics" and a contributor to pediatric literature over a period of many years. Among his numerous medical honors was the presidency of the American Pediatric Society in 1930, and honorary membership in the British Pediatric Society.

Dr. Lee Forrest Hill of Des Moines, Iowa, has been appointed to the American Board of Pediatrics as one of the three members from the Academy.

Dr. A. L. Van Horn has been appointed Chief of the Division of Health Services of the Children's Bureau succeeding Dr. Edwin F. Daily who has entered the Army. Dr. Betty Ruse succeeds Dr. Van Horn as Assistant Director for Crippled Children.

Dr. Alexander T. Martin of New York and Dr. Hugh McCulloch of St. Louis have been appointed representatives of the American Academy of Pediatricians on the recently formed Council on Rheumatic Fever.

Dr. Rupert R. Rogers of Warren, Ohio, died April 20, 1944.

Dr. David H. Boyd, Pittsburgh, Pa., died July 14, 1944.

The *American Board of Pediatrics* announces that all places for the examinations in St. Louis and New York this fall have been filled and no more candidates can be accepted.

The *American Board of Pediatrics* announces the following schedule for the spring of 1945:

Written examination: locally under a Monitor, March 2, 1945.

Oral examinations: New York City, April 14 or 15, 1945; closing date for applications, Dec. 15, 1944.

Chicago, May 19 or 20, 1945; closing date for applications, Jan. 19, 1945.